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(54) Title: SUBSTITUTED AMINOALKYLAMIDE DERIVATIVES AS ANTAGONISTS OF FOLLICLE STIMULATING HORMONE

(57) Abstract: The present invention is directed to a series of novel substituted aminoalkylamide derivatives, pharmaceutical compositions containing them and their use in the treatment of reproductive disorders and affective conditions. Further, the compounds of the invention are antagonists of follicle stimulating hormone, a hormone associated with the human reproductive system.

SUBSTITUTED AMINOALKYLAMIDE DERIVATIVES AS ANTAGONISTS OF FOLLICLE STIMULATING HORMONE

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims priority from United States provisional application Serial No. 60/173,139, filed December 27, 1999, the contents of which are hereby incorporated by reference.

FIELD OF THE INVENTION

This invention relates to novel substituted aminoalkylamide derivatives, pharmaceutical compositions containing them and their use in the treatment of reproductive disorders and affective conditions. The compounds of the invention are antagonists of follicle stimulating hormone, a hormone associated with the human reproductive system.

BACKGROUND OF THE INVENTION

Follicle stimulating hormone (FSH) belongs to a family of glycoprotein hormones, which includes lutenizing hormone (LH), thyrotropin (TSH) and chorionic gonadotropin (CG). Each of these hormones is composed of two different non-covalently bound subunits termed α and β. Within a species the amino acid sequence of the α subunits for these different hormones is identical, while the hormone specific β subunits exhibit different amino acid sequences (Combarnous, Endocrine Review, **13**:670-691 (1992).

In females, follicle stimulating hormone (FSH) stimulates follicular granulosa cell proliferation in the ovary and impacts synthesis of estrogen, a hormone which is integral to follicular maturation and ovulation. An antagonist of FSH therefore acts to limit proliferation of follicular granulosa cells in the ovary, acting as a contraceptive. The FSH antagonist may also delay the maturation of follicles within the ovary, thereby postponing the maturation of a limited number of follicles in women. Such treatments have the potential for increasing the possibility of natural fertilization and pregnancy later in life.

Because of the controlling function of FSH on estrogen synthesis, an FSH antagonist may also be effective in the treatment of estrogen related disorders such as uterine fibroids, endometriosis, polycystic ovarian disease, dysfunctional uterine bleeding, breast cancer and ovarian cancer.

An added advantage for an FSH antagonist would be its specific action on ovarian tissue without impact on peripheral tissues containing estrogen receptors. This would be expected to reduce the side effects associated with estrogen receptor antagonists.

Because the proliferation of follicular granulosa cells also impacts the health and development of the oocyte, FSH antagonists may be useful in preventing depletion of oocytes, a common side effect of chemotherapy or similar treatments designed to treat rapidly dividing cells.

In males, follicle stimulating hormone (FSH) is involved in the maturation of sperm cells. More specifically, FSH action in males is directed at the Sertoli cells, which are a recognized target of the hormone and which support the process of sperm maturation (spermatogenesis). FSH antagonists will therefore inhibit sperm maturation without affecting the production of androgens produced from Leydig cells under the control of luteinizing hormone (LH). In addition, FSH receptors have been reported in the epididymis in the male reproductive tract. Thus an FSH antagonist would be expected to affect the viability and motility of sperm by controlling functions of the epididymis.

FSH antagonists also have the potential to modify the rate of germ cell division in males. Because chemotherapy is known to deplete rapidly dividing cells such as spermatocytes, an FSH antagonist may be useful in a planned chemotherapy regimen to prevent spermatocyte depletion.

An FSH antagonist used as a female contraceptive could be used in contraceptive formulations alone or in combination with known contraceptive agents such as progesterone receptor modulators, estrogen receptor modulators, or androgen receptor modulators. An FSH antagonist used as a male contraceptive could be used alone or in combination with androgen receptor modulators, progesterone receptor modulators, or with estrogen receptor modulators. In addition, agents that affect the viability or motility or fertilizability of sperm by acting within the female genital tract may also be used

in combination with FSH antagonists concomitantly, or as scheduled in a kit that prevents fertilization during the administration of an FSH antagonist. An example of such an agent is nonoxynol-9.

In recent years, peptide (based) FSH agonists and antagonists have been discovered and developed. Bono, G., et. al., in WO 97/12038 disclose novel amino acid residue peptide useful in stimulating FSH enhancement.

Amino acid based sulfonamide derivatives have also been developed for the treatment of a variety of conditions and disorders. Dumont, R. in WO 93/05014 discloses sulfonamide derivatives useful as inhibitors of Ca^{+2} dependent enzymes.

The compounds of the present invention are non-peptide antagonists of FSH useful in the treatment of estrogen related disorders such as uterine fibroids, endometriosis, polycystic ovarian disease, dysfunctional uterine bleeding, breast cancer and ovarian cancer; prevention of depletion of oocytes (a common side effect of chemotherapy or similar treatment); female and male contraception; and prevention of spermatocyte depletion.

Additionally, the generation of chemical libraries on and off solid resins has proven to be a valuable resource for the pharmaceutical industry in their endeavors to discover new drugs using high throughput screening (HTPS) techniques. In creating the libraries, the compounds are ideally synthesized in situ in solution phase or on a solid support. However, relatively simple synthetic methods to produce a diverse collection of such derivatives in situ are often not available.

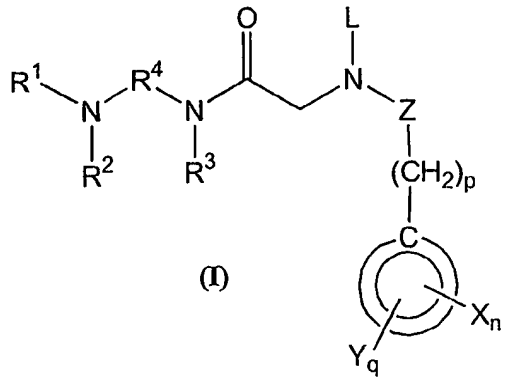
Pharmaceutical drug discovery relies heavily on studies of structure-activity relationships wherein the structure of "lead compounds" is typically altered to determine the effect of such alteration on activity. Alteration of the structure of the lead compounds permits evaluation of the effect of the structural alteration on activity.

Thus, libraries of compounds derived from a lead compound can be created by including derivatives of the lead compound and repeating the screening procedures. In this manner, compounds with the best biological profile, i.e., those that are most active and which have the most ideal

pharmacologic and pharmacokinetic properties, can be identified from the initial lead compound.

SUMMARY OF THE INVENTION

The present invention is directed to compounds of the formula (I)



(I)

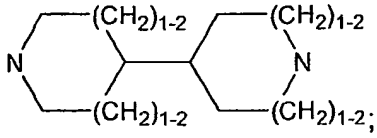
wherein

R^1 and R^2 are independently selected from the group consisting of hydrogen, C_1-C_6alkyl, C_1-C_6alkylcarbonyl, C_1-C_6perhaloalkyl, phenyl, phenylC_1-C_6alkyl-, phenylcarbonyl-, pyridyl, pyridylC_1-C_6alkyl-, pyridylcabonyl-, thienyl, thienylC_1-C_6alkyl- and thienylcarbonyl, wherein the phenyl, pyridyl or thienyl is optionally substituted with one to three substituents independently selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy or NO_2;

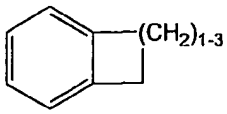
R^3 is selected from the group consisting of hydrogen, C_1-C_6alkyl, C_2-C_4alkenyl and C_2-C_4alkynyl, where the C_1-C_6alkyl is optionally substituted with a phenyl, pyridyl, thienyl or furyl, wherein the phenyl, pyridyl, thienyl or furyl is optionally substituted with one to three substituents independently selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy or NO_2;

R^4 is selected from the group consisting of -C_2-C_6alkyl-, -cyclopentyl-, -cylcohexyl-, -cyclohexyl-CH_2-, -CH_2-cyclohexyl-CH_2-, –CH_2-phenyl-CH_2-, -C(O)-CH_2-phenyl-CH_2-, -C(O)-C_1-C_6alkyl- and –cyclohexyl-CH_2-cyclohexyl-;

where the R^4 substituent is inserted into the compound of formula (I) from left to right, as defined;

alternately, R^2, R^3, and R^4 can be taken together with the two N atoms of the diamine portion of the molecule to form  ;

alternately, R^3 can be taken together with R^2 as -C_2-C_3alkyl-, provided that R^4 is -C_2-C_6alkyl-;

L is selected from the group consisting of –C_3-C_6cycloalkyl (wherein the cycloalkyl is substituted with R^5 and R^6), a bicyclic compound of the form  (wherein the point of the attachment of the bicyclic compound is any carbon atom of the alkyl portion and wherein the aromatic portion of the bicyclic compound is optionally substituted with one to three substituents independently selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy, NO_2, acetamido, -NH_2, -NH(C_1-C_6alkyl) or -N(C_1-C_6alkyl)$_2$), and –$(CH_2)_m$-$CR^8R^5R^6$;

m is 0 to 3;

R^5 is selected from the group consisting of phenyl, naphthyl, (wherein the phenyl and naphthyl may be optionally substituted with one to three substituents independently selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy, NO_2, acetamido, -NH_2, -NH(C_1-C_6alkyl), -N(C_1-C_6alkyl)$_2$, C_1-C_6alkylcarbonylamino or C_1-C_6alkylsulfonylamino), bicyclo[4.2.0]octa-1,3,5-trienyl, 2,3-dihydro-1H-indolyl, N-methylpyrrolidinyl, 3,4-methylenedioxyphenyl, C_3-C_6cyloalkenyl, (wherein the cycloalkenyl group contains one or two double bonds), a six membered heteroaryl (wherein the six membered heteroaryl contains one to three N atoms), and a five membered heteroaryl (wherein the five membered heteroaryl contains one sulfur, oxygen or nitrogen, optionally contains one to three additional nitrogen atoms); wherein the point of attachment for the five or six membered heteroaryl is a carbon atom; and wherein the five or six membered heteroaryl is optionally substituted with one to three substituents independently selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy or NO_2;

R^6 is selected from the group consisting of hydrogen, C_1-C_6alkyl, C_3-C_6cycloalkyl, C_1-C_6alkoxy, hydroxy and phenyl, (wherein the phenyl may be optionally substituted with one to three substituents independently selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl or trifluoromethoxyl); provided that R^6 may be phenyl only when R^5 is phenyl;

R^8 is selected from the group consisting of hydrogen and C_1-C_6alkyl;

Z is selected from the group consisting of $-SO_2-$, -C(=O)-, and –C(=O)NH-;

p is 0 to 1;

 is selected from the group consisting of phenyl, naphthyl, quinolinyl, thienyl, and furyl;

X is selected from the group consisting of halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy, NO_2, acetamido, $-NH_2$, -NH (C_1-C_6alkyl) and $-N(C_1$-C_6alkyl$)_2$;

n is 0 to 3;

Y is selected from the group consisting of phenyl, -O-phenyl, -NH-phenyl, naphthyl, (wherein the phenyl or naphthyl is optionally substituted with one to three substituents selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy, NO_2, cyano, methylthio, acetamido, formyl, -amino, -aminocarbonyl, -NH-C_1-C_6alkyl, $-N(C_1$-C_6alkyl$)_2$, -COOH, -COO(C_1-C_6alkyl), -COO(C_1-C_6alkylphenyl), C_1-C_6alkylcarbonylamino, C_1-C_6alkylaminocarbonyl, di(C_1-C_6alkyl)aminocarbonyl, aminosulfonyl, C_1-C_6alkylaminosulfonyl or di(C_1-C_6alkyl)aminosulfonyl), biphenyl, 3,4-methylenedioxyphenyl, dianthrenyl, dibenzothienyl, phenoxathiinyl, a six membered heteroaryl (wherein the six membered heteroaryl contains one to three nitrogen atoms), and a five membered heteroaryl (wherein the five membered heteroaryl contains one sulfur, oxygen or nitrogen atom, optionally contains one to three additional nitrogen atoms); wherein the point of attachment for the five or six membered heteroaryl is a carbon atom; and wherein the five or six membered heteroaryl is optionally substituted with one to three substituents selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy,

trifluoromethyl, trifluoromethoxy, formyl, NO_2, cyano, methylthio, acetamido, -amino, -aminocarbonyl, -NH C_1-C_6alkyl, -N(C_1-C_6alkyl)$_2$, -COOH, -COO(C_1-C_6alkyl), or -COO(C_1-C_6alkylphenyl));

q is 0 to 1;

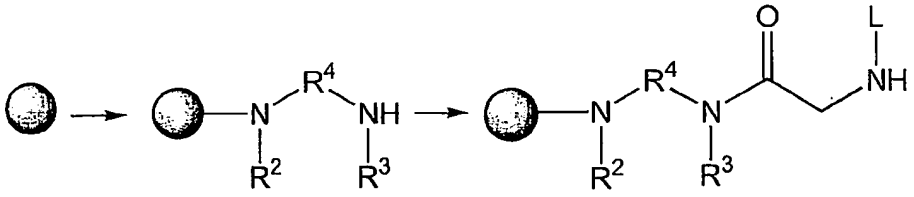
provided that when q is 1, n is 0;

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

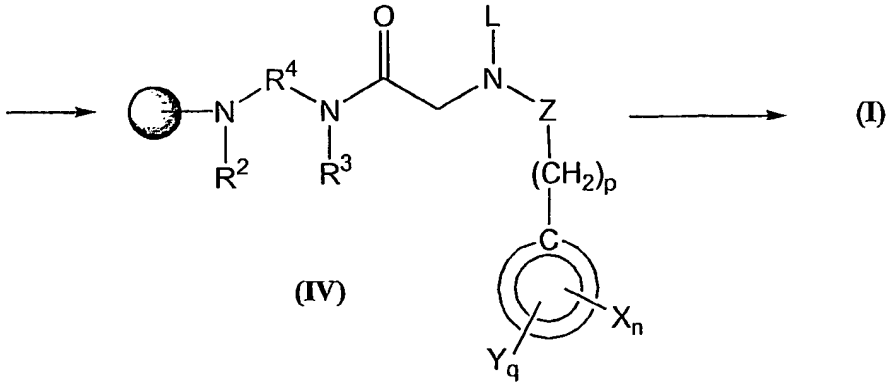
DETAILED DESCRIPTION OF THE INVENTION

The compounds of formula (I) that comprise this invention may be prepared using a process wherein the compound is synthesized on a solid support resin, followed by cleavage of the compound from the resin support, as a final isolation step. The various substituents described in formula (I) may be present initially on the reagents employed to prepare the compounds of formula (I). In some instances they may be conveniently added following cleavage. In those cases where the substituents are present on the reagents, care must be taken in the selection of the resin to insure that the substituents are compatible with the selected resin.

One method for producing the compounds of formula (I) involves synthesis, on resin, of three intermediates, followed by cleavage of the resin to yield the desired product, as outlined in Scheme 1.



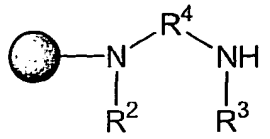
(II) (III)



Scheme 1

The solid support resin, herein represented by the symbol  , is typically polystyrene, and is terminated with a reactive functional group. There are a number of commercially available resins, with a variety of terminating groups. Suitable examples of support resins for preparation of compounds of formula (I) include: Wang resin (Wang, S. S., J. Am. Chem. Soc., 95, 1328 (1973); Kiselov, A. S. and Amstrong, R. W., Tetrahedron Letter, 318, 6163 (1997)), [wherein the terminating group is –(p-phenyl)-CH_2-O-(p-phenyl)-CH_2-OH]; RAPP Tentagel SAM resin (Rotte, B., et.al., Collect. Czech. Chem. Commun., 61, 5304 (1996)), [wherein the terminating group is –(p-phenyl)-CH_2-O-(p-phenyl)-CH_2-NH_2]; vinylsulfonyl resin (Kroll, F. E., et. al., Tetrahedron Lett., 38, 8573, 1997), [wherein the terminating group is –(p-phenyl)–CH_2-SO_2-CH=CH_2]; rink amide resin (Rink, H., Tetrahedron Lett., 28, 3787, 1987; Brown, E. G. and Nuss, J. M., Tetrahedron Lett., 38, 8457, 1997), [wherein the terminating group is -CH_2-O-(p-phenyl)-CH_2(NH-Fmoc)-(2,4-dimethoxyphenyl)]; FMPB resin (4-(4-formyl-3-methoxyphenoxy)butyryl AM resin) (Bilodeau, M. T. & Cunningham, A. M., J. Org. Chem., 63, 2800, 1998; Kearny, P. T., et. al., J. Org. Chem., 63, 196, 1998) [wherein the terminating group is an aldehyde]; and the like. The appropriate selection of solid support resin and terminating group is based on the synthesis steps, reaction conditions and final compound substituents; and may be determined by one skilled in the art.

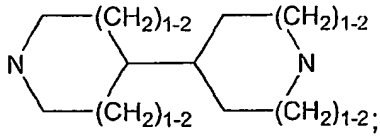
The selected resin and appropriate reactants are employed to prepare resin bound, substituted diamines of formula (II):



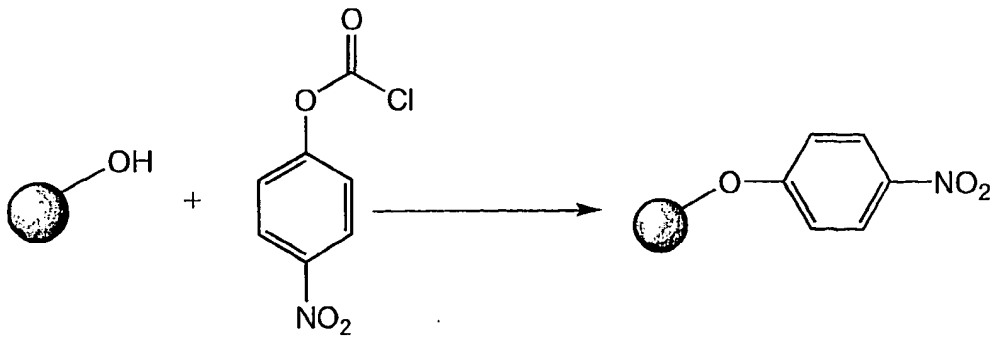
(II)

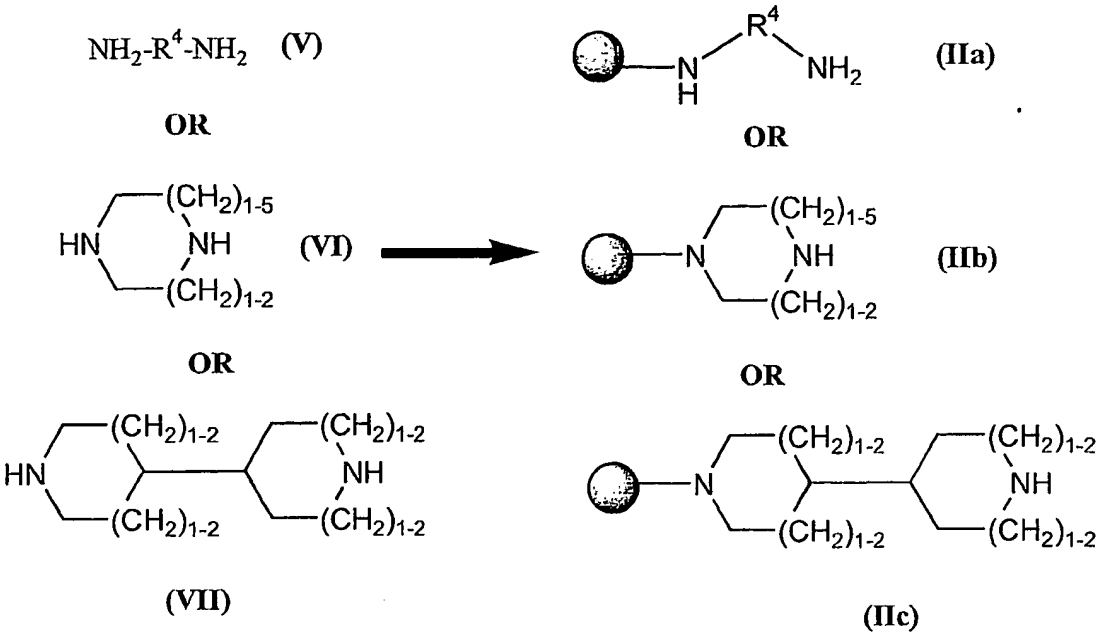
Broadly, there are three approaches described herein to obtain the resin bound substituted diamines of formula (II). In the first approach a commercial resin capable of direct coupling reactions to an appropriately substituted diamine is purchased and reacted to produce the compound of formula (II). In the second approach, a commercial resin is suitably activated to react with an appropriately substituted diamine. This approach is advantageously employed in those cases where the purchased resin is not amine terminated. In the third approach, a commercially available amine terminated resin is reacted with a substituted and protected amine alcohol to form the resin substituted diamine of formula (II). In this third approach, the terminal amine of the selected resin is incorporated into the end product compound.

Specifically, compounds of formula (II) wherein R^2 and R^3 are hydrogen; wherein R^2 and R^3 are taken together as $-C_2$-C_3alkyl and R^4 is other than C(O)-CH_2-phenyl-CH_2- or C(O)-C_1-C_6alkyl-; and wherein R^2, R^3 and R^4 are taken together with the two N atoms of the diamine portion of the molecule to form



; may be prepared as outlined in Scheme 2 below:



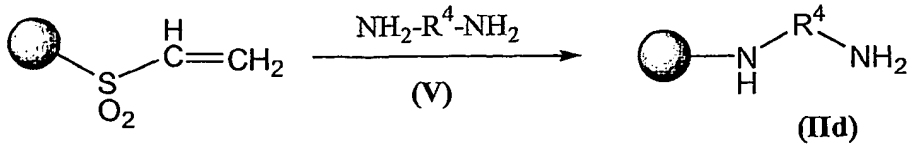


SCHEME 2

According to Scheme 2, a commercially available, OH terminated resin is coupled with 4-nitrophenyl chloroformate, in an organic solvent such as DCM, DCE, and the like, preferably DCM, in the presence of an amine base, such as pyridine, N-methylmorpholine (NMM), triethylamine (TEA), diisopropylethylamine (DIEA), and the like, preferably N-methylmorpholine (NMM), preferably at room temperature, to incorporate the –C(O)-O-(p-nitrophenyl)- group into the resin, to form the corresponding *p*-nitrophenol carbonate terminated resin.

The *p*-nitrophenol group on the p-nitrophenol carbonate terminated resin is next displaced with a suitably substituted linear diamine of formula (V), a suitably substituted cyclic diamine of formula (VI), or a suitably substituted bicyclic heterocyclyl diamine of formula (VII), in an organic solvent such as DMF, DMAC, DCM, DCE, and the like, preferably at room temperature, to form the corresponding resin bound substituted diamine of formula (IIa), (IIb) or (IIc), respectively.

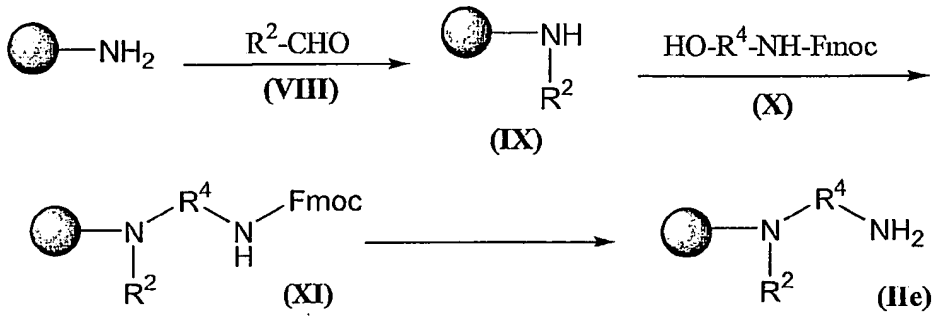
Alternately, compounds of formula (II), wherein R^2 and R^3 are hydrogen may be prepared according to the process outlined in Scheme 3.



SCHEME 3

Accordingly, a commercially available, vinylsulfonyl terminated resin is coupled with a suitably substituted linear diamine of formula (V), in an organic solvent such as DMF, overnight, at room temperature, to produce the resin bound substituted diamine of formula (IId). In this approach, the amine group is coupled directly to the terminal methylene group of the vinylsulfonyl terminated resin.

Compounds of formula (II) wherein R^3 is hydrogen and R^4 is selected from C(O)-CH_2-phenyl-CH_2- or C(O)-C_1-C_6alkyl- may be prepared according to the process outlined in Scheme 4.

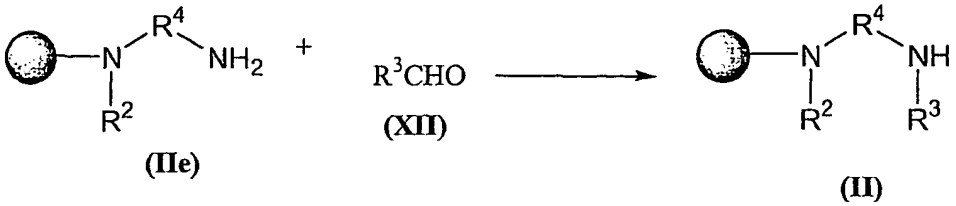


SCHEME 4

When R^2 is other than hydrogen, a commercially available amine terminated resin is reacted with a suitably substituted aldehyde of formula (VIII), in an organic solvent such as DCM, DCE, and the like, in the presence of a catalyst such as sodium cyanoborohydride, sodium triacetoxyborohydride and the like, preferably sodium triacetoxyborohydride, preferably at room temperature, to produce the corresponding substituted amine terminated resin of formula (IX).

The substituted amine terminated resin of formula (IX) is coupled with a suitably substituted Fmoc-protected amine alcohol, a compound of formula (X), in an organic solvent such as DMF, DMAC, DCM, and the like, preferably DMF, preferably at room temperature, to produce the corresponding resin bound Fmoc-protected, substituted diamine of formula (XI). The Fmoc protecting group on the resin bound substituted diamine of formula (XI) is then removed using 20% piperidine in DMF, preferably at room temperature, to produce the corresponding resin bound, substituted diamine of formula (IIe).

Compounds of formula (II) wherein R^3 is other than hydrogen may be prepared according to the process outlined in Scheme 5.

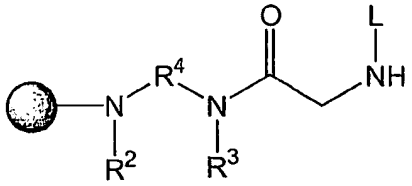


(IIe) (II)

SCHEME 5

A resin bound substituted diamine of formula (IIe) is coupled with a suitably substituted aldehyde of formula (XII), in the presence of a reducing agent such as sodium cyanoborohydride, sodium triacetoxyborohydide, and the like, preferably triacetoxyborohydride, in an organic solvent such as DCM, DCE, and the like, preferably DCE, preferably at room temperature, to produce the corresponding resin bound substituted diamine of formula (II).

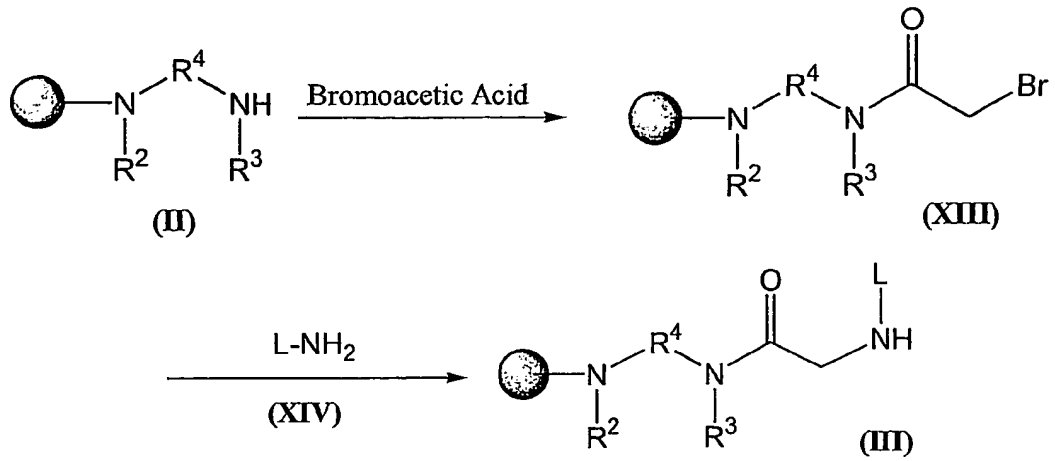
The resin bound, substituted diamines of formula (II) are next reacted with suitably substituted reagents to produce the corresponding resin bound, substituted secondary amine of formula (III):



(III)

In a general approach to producing the resin bound substituted triamine of formula (III), bromoacetic acid is initially coupled to the diamine for formula (II), followed by coupling of a suitably substituted amine.

More specifically, in this approach, compounds of formula (III) may be prepared according to the process outlined in Scheme 6. This approach is also particularly advantageous in the preparation of compounds of formula (I) wherein L is $-C_3$-C_6cycloalkyl.

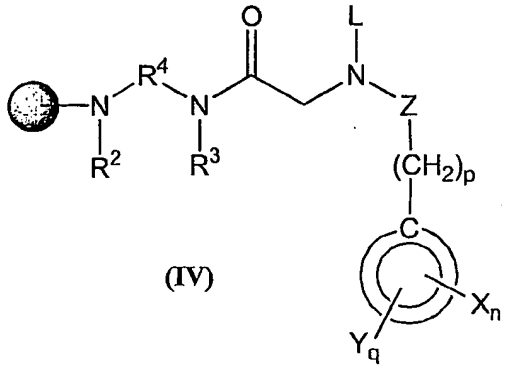


SCHEME 6

Accordingly, a resin bound, substituted diamine of formula (II) is coupled with bromoacetic acid, using a coupling agent such as diisopropyl carbodiimide, 1,1'-carbonyldiimidazole, N,N'-dicyclohexylcarbodiamide, and the like, preferably diisopropylcarbodiamide, in a solvent such as DMF, DMAC, and the like, preferably DMF, preferably at room temperature, to form the corresponding resin bound, bromoacetylated alkylcarbonyl diamine of formula (XIII).

The bromine on the resin bound, bromoacetylated alkylcarbonyl diamine of formula (XIII) is then displaced with a suitably substituted amine of formula (XIV), in a solvent such as DMSO, preferably at room temperature, to form the corresponding resin bound, substituted secondary amine of formula (III).

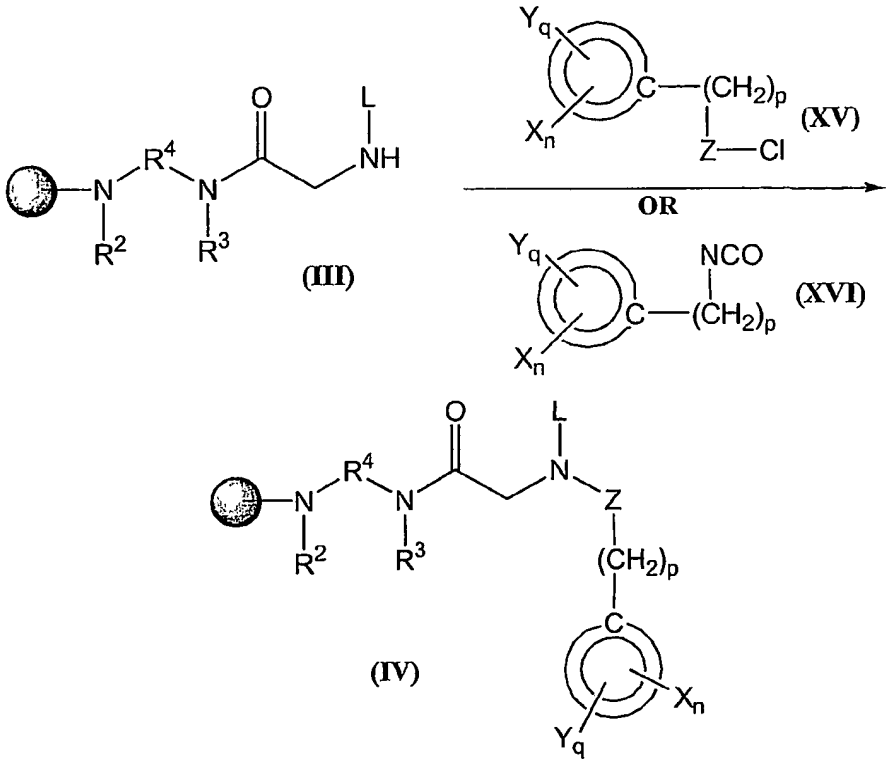
The resin bound, substituted secondary amine of formula (III) is subsequently reacted with suitably substituted reagents to produce the corresponding resin bound, compound of formula (IV):



The resin bound compound of formula (IV) may be prepared via two processes. In the first process, the resin bound, substituted secondary amine

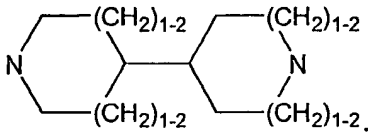
of formula (III) is directly coupled with a suitably substituted sulfonyl chloride, suitably substituted carbonyl chloride or suitably substituted isocyanate reagent to prepared the end product compound. In the second process, the resin bound, substituted secondary amine of formula (III) is first coupled with a halogen substituted aryl or heteroaryl sulfonyl chloride, followed by displacement of the halogen with a suitably substituted aryl or heteroaryl substituted boronic acid, to yield the end product compound.

More particularly, in the first process, the resin bound compound of formula (IV) is prepared as outlined in Scheme 7.

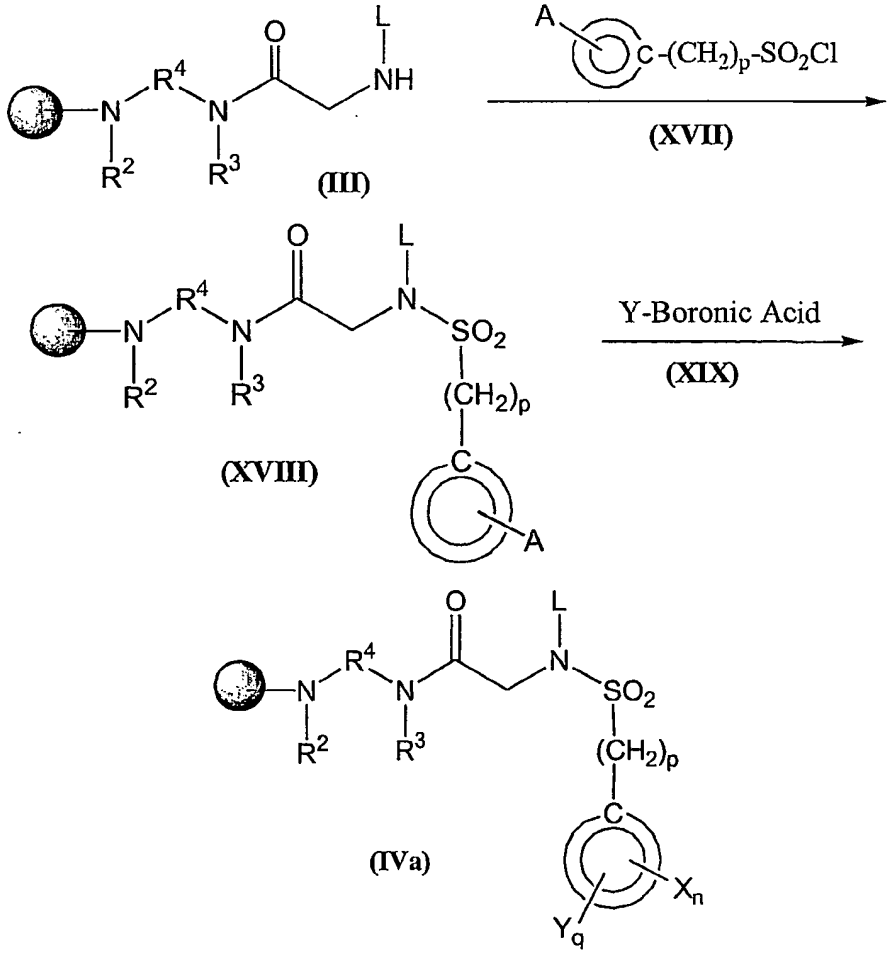


Scheme 7

According to the first process, the resin bound, substituted secondary amine of formula (III) is coupled with a suitably substituted chloride of formula (XV), or a suitably substituted isocyanate of formula (XVI), in a solvent such as DCM, DCE, chloroform, and the like, preferably DCM, in the presence of an amine base such as pyridine, N-methylmorpholine (NMM), triethyl amine (TEA), diisopropylethylamine (DIEA), and the like, preferably pyridine, preferably at room temperature, to form the corresponding resin bound compound of formula (IV).

The second process is particularly advantageous for preparation of compounds of formula (I) wherein Z is sulfonyl, n is 0, q is 1 and the  substituent is phenyl, napthyl, thienyl or furyl. The second process is also particularly advantageous for preparation of compounds of formula (I) wherein R^2 and R^3 are taken together as C_2-C_3alkyl and Z is sulfonyl; and wherein R^2, R^3, and R^4 are taken together with the two N atoms of the diamine portion of the molecule to form  .

In the second process, the resin bound compound of formula (IV) is prepared via the process outlined in Scheme 8.



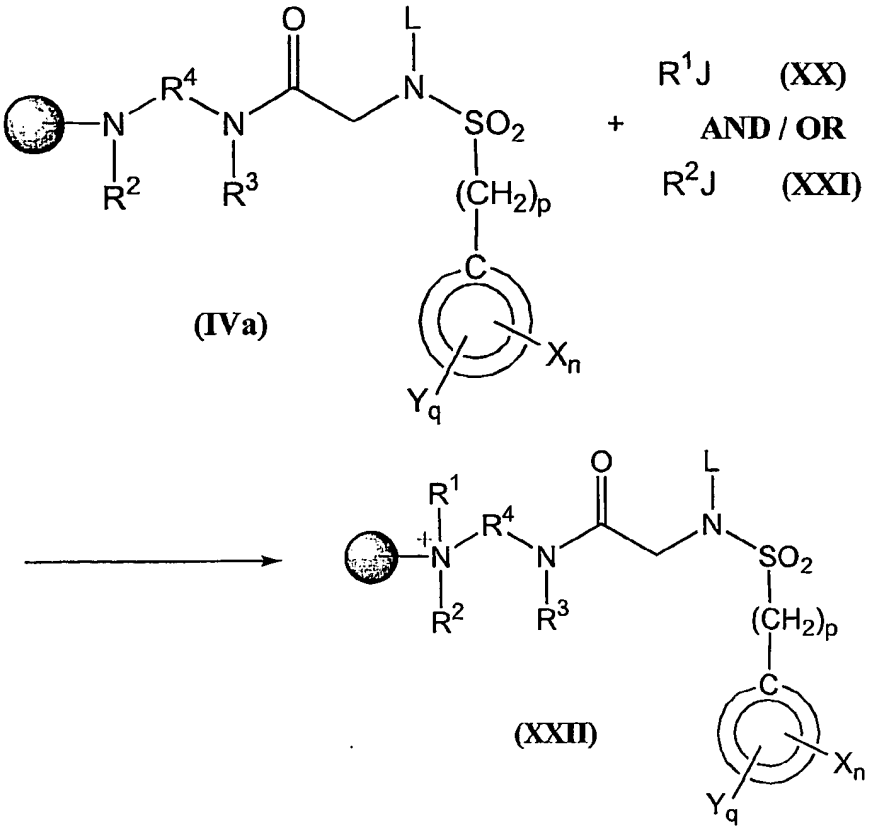
Scheme 8

The resin bound, substituted secondary amine of formula (III) is coupled with a suitably substituted aryl or heteroaryl sulfonyl chloride of formula (XVII), wherein A represents a halogen selected from chlorine, bromine or iodine, preferably bromine, in a solvent such as DCM, DCE, chloroform, and the like, preferably DCM, in the presence of an amine base such as pyridine, N-methylmorpholine, triethylamine (TEA), diisopropylethylamine (DIEA), and the like, preferably pyridine, preferably at room temperature, to form the corresponding resin bound, substituted sulfonyl compound of formula (XVIII).

On the resin bound, substituted sulfonyl of formula (XVIII), the halogen represented by A is next displaced with a suitably substituted boronic acid of formula (XIX), using Suzuki conditions (in a solvent such as dimethoxyethane (DME), dioxane, and the like, in the presence of a base such as 2M sodium carbonate, tetramethylguanadine (TMG), and the like, under a N_2 atmosphere, at a temperature in the range of about 80-100°C, in the presence of a catalyst, such as palladium tetrakistriphenylphosphine), to form the corresponding resin bound, substituted sulfonamide formula (IVa).

The resin bound compound of formula (IV), may next be treated to yield the corresponding compound of formula (I) by cleaving the solid support resin, using a cleaving cocktail, such as 90:10 TFA:water, preferably at room temperature, to produce the corresponding compound of formula (I).

A resin bound compound of formula (IVa) may alternatively be further reacted with a suitably substituted compound of formula (XX) and / or formula (XXI), wherein J is bromine or iodine, to incorporate R^1 and R^2 substituents, wherein $R^1 = R^2$ and are other than hydrogen. For this process, the preferred resin is the vinylsulfonyl terminated resin, R^4 is other than $-C(O)-CH_2$-phenyl- or $-C(O)-C_1-C_6$alkyl-, and the R^1 and R^2 substituents are incorporated according to the process outlined in Scheme 9.

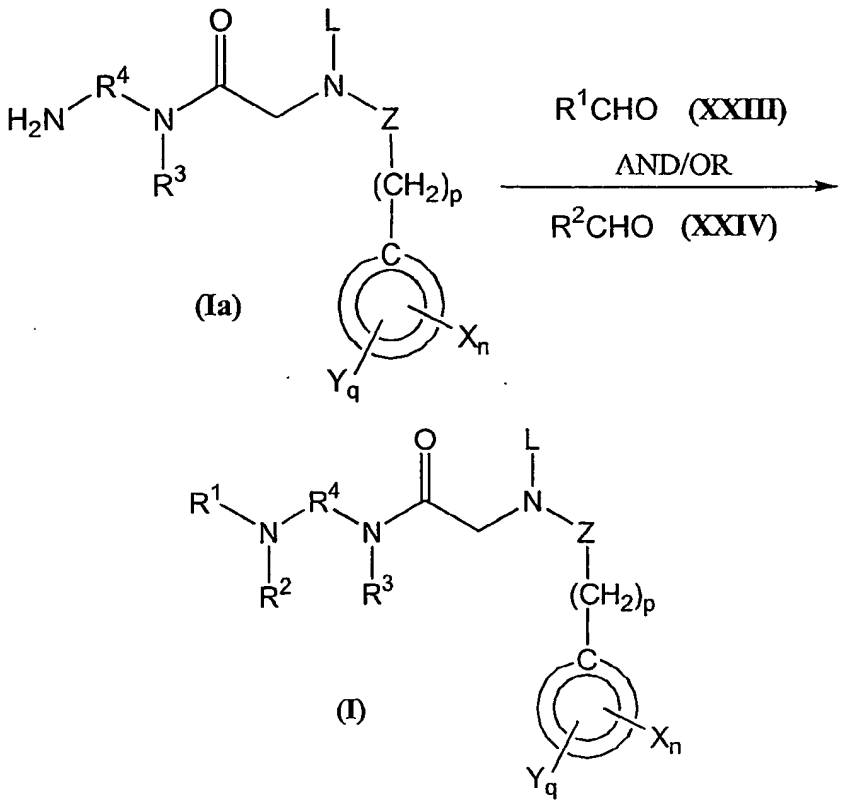


Scheme 9

Accordingly, a resin bound compound of formula (IVa) is reacted with a suitably substituted compound of formula (XX) and / or formula (XXI), wherein J is bromine or iodine, preferably at room temperature, to produce the corresponding resin bound, quaternary amine of formula (XXII).

The resin bound quaternary amine of formula (XXVI) is then treated to yield the desired corresponding compound of formula (I) by cleaving the solid support resin, using a cleaving cocktail, such as 20% DIEA in DMF, preferably at room temperature, to produce the corresponding compound of formula (I).

In an alternative scheme for producing compounds of formula (I) wherein R^1 and/or R^2 are other than hydrogen, the R^1 and R^2 substituents may be introduced following cleavage of the resin bound compound of formula (IV). More particularly, such a process is as outlined in Scheme 10.



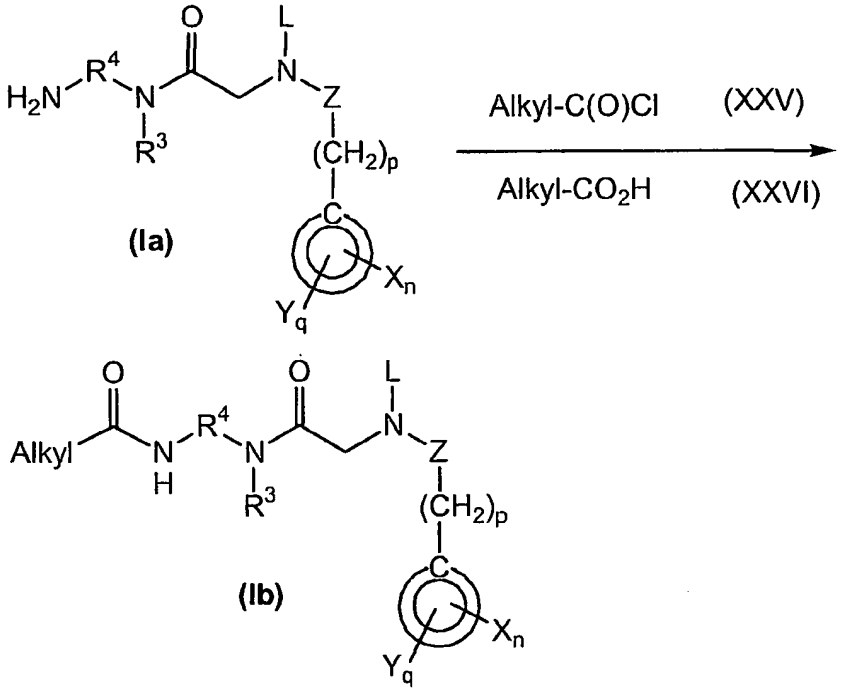
Scheme 10

A compound of formula (Ia), wherein R^1 and R^2 are hydrogen, is treated with a suitably substituted aldehyde of formula (XXIII), preferably in the amount of at least one molar equivalent, in an organic solvent such as TMOF, and the like, in the presence of a reducing agent such as sodium triacetoxyborohydride, and the like, preferably at room temperature, and then with a suitably substituted aldehyde of formula (XXIV), preferably in the amount of at least one molar equivalent, in an organic solvent such as TMOF, and the like, in the presence of a reducing agent such as sodium triacetoxyborohydride, and the like, preferably at room temperature, to produce the corresponding compound of formula (I).

In an alternative method of Scheme 10, compounds of formula (I), wherein R^1 and R^2 are the same and other than hydrogen, are produced by treating the compound of formula (Ia) with at least two molar equivalents of a suitably substituted aldehyde of formula (XXIII) or (XXIV), to produce the corresponding product of formula (I).

In another alternative method of Scheme 10, compounds of formula (I), wherein one of R^1 or R^2 is hydrogen, the compound of formula (Ia) is treated with at least one molar equivalent of a suitably substituted aldehyde of formula (XXIII) or (XXIV), to yield the desired corresponding compound of formula (I).

Compounds of formula (I), wherein R^1 and/or R^2 is alkylcarbonyl may be prepared according to the process outlined in Scheme 11.



Scheme 11

Accordingly, a suitably substituted compound of formula (Ia), wherein R^1 and R^2 are each hydrogen, is treated with a suitably substituted acid chloride of formula (XXV), preferably in the amount of at least one molar equivalent, in an organic solvent such as chloroform, DCM, and the like, in the presence of a organic base such as TEA, and the like, preferably at room temperature, to yield the corresponding compound of formula (Ib). Alternatively, a suitably substituted compound of formula (Ia), wherein R^1 and R^2 are each hydrogen, is treated with a suitably substituted carboxylic acid of formula (XXVI), preferably in the amount of at least one molar equivalent, in an organic solvent such as DMF, and the like, in the presence of a coupling agent such as DIC, and the like, preferably at room temperature, to yield the corresponding compound of formula (Ib).

As used herein, unless otherwise noted, "alkyl" whether used alone or as part of a substituent group, shall include straight and branched chains containing 1 to 6 carbon atoms. For example, alkyl radicals include methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, t-butyl, pentyl, 2-methyl-3-butyl, hexyl and the like. Similarly, the term "cycloalkyl" shall include saturated alkyl ring structures containing 3 to 6 carbon atoms. Suitable examples include cyclopropyl, cyclobutyl, cyclopentyl and cylcohexyl.

As used herein, unless otherwise noted, "alkenyl" and "alkynyl" shall include straight and branched chain alkene and alkyne having 1 to 6 carbon atoms, for example allyl, vinyl, 2-propenyl, 2-propynyl, and the like.

As used herein, unless otherwise noted, "alkoxy" shall denote an oxygen ether radical of the above described straight or branched chain alkyl groups. For example, methoxy, ethoxy, propoxy, sec-butoxy, t-butoxy, 2-methyl-3-bytoxy and the like.

As used herein the terms "aromatic and aryl" shall denote phenyl and naphthyl.

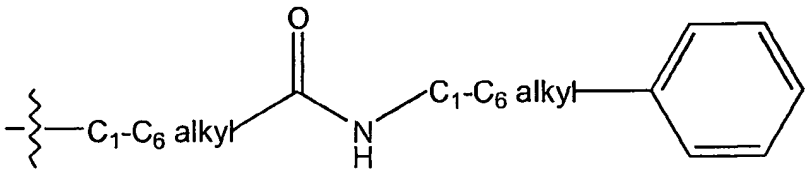
Suitable "six membered heteroaryls containing one to three nitrogen atoms" include pyridyl, pyridizanyl, pyrimidinyl, pyrazinyl, 1,3,5-triazinyl, 1,2,4-triazinyl and 1,2,3-triazinyl.

Suitable "five membered heteroaryl containing one sulfur, oxygen or nitrogen atom, optionally containing one to three additional nitrogen atoms" include thienyl, furyl, pyrrolyl, thiazolyl, isothiazolyl, thiadiazolyl, oxazolyl, isoxazolyl, 1,2,3-oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3,4-oxatriazolyl, 1,2,3,5-oxatriazolyl, imidazolyl, pyrazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, and the like.

As used herein, unless otherwise noted, "halogen" shall denote chlorine, bromine, fluorine and iodine.

As used herein, unless otherwise noted, "*" represents the presence of a stereogenic center.

Under standard nomenclature used throughout this disclosure, the terminal portion of the designated side chain is described first, followed by the adjacent functionality toward the point of attachment. Thus, for example, a "phenylC_1-C_6alkylamidoC_1-C_6alkyl" substituent refers to a group of the formula



In a preferred embodiment of the present invention are compounds of the formula (I) wherein

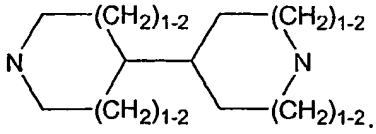
R^1 and R^2 are independently selected from the group consisting of hydrogen, methyl, ethyl, methylcarbonyl, trifluoromethyl, phenyl, benzyl, phenylcarbonyl, pyridyl, pyridylcarbonyl, thienyl, thienylmethyl and thienylcarbonyl (where the phenyl, pyridyl or thienyl is optionally substituted with one to two substituents independently selected from halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl, trifluoromethoxy or nitro); and

R^3 is selected from the group consisting of hydrogen, methyl, -CH=CH- (optionally substituted with phenyl, pyridyl or thienyl; wherein the phenyl, pyridyl or thienyl is further optionally substituted with one to two substituents independently selected from the group consisting of halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl, trifluoromethoxy and nitro), -C≡C-, (optionally substituted with phenyl, pyridyl or thienyl; wherein the phenyl, pyridyl or thienyl is further optionally substituted with one to two substituents independently selected from the group consisting of halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl, trifluoromethoxy and nitro).

More preferably, R^1, R^2, and R^3 are the same; most preferably R^1, R^2 and R^3 are the same and are hydrogen.

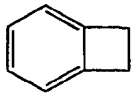
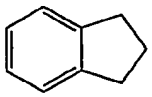
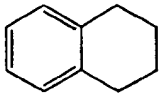
In another preferred embodiment of the present invention are compounds of the formula (I) wherein R^2 and R^3 are taken together as C_2-C_3alkyl, more preferably 1,2-ethyl; and R^4 is C_2-C_6alkyl, more preferably 1,2-ethyl or 1,3-n-propyl.

In another preferred embodiment of the present invention are compounds of the formula (I) wherein R^2, R^3, and R^4 are taken together with the two N atoms of the diamine portion of the molecule to form



Preferred R^4 substituents include $-C_2$-C_6alkyl, -cyclohexyl, -CH_2-cyclohexyl-CH_2, -cyclohexyl-CH_2-cyclohexyl and $-CH_2$-phenyl-CH_2.

In another preferred embodiment of the invention are compounds of the formula (I) wherein R^2, R^3, and R^4 may be taken together with the two N atoms of the diamine portion of the molecule to form 4,4'-bipiperidinyl.

Preferred L substituents include –cyclopropyl-, cyclohexyl-, (wherein the cylcopropyl or cyclohexyl is substituted with R^5 and R^6),  ,  ,  , and $(CH_2)_m$-$CR^8R^5R^6$.

Preferred R^5 substituents include phenyl (wherein the phenyl is optionally substituted with one to two substituents independently selected from halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl, trifluoromethoxy, methylcarbonylamino, methylsulfonylamino, nitro, acetomido, amino, C_1-C_3alkylamino or di(C_1-C_3alkyl)amino), N-methylpyrrolidinyl, 3,4-methylenedioxyphenyl, bicyclo[4.2.0]octa-1,3,5-trienyl, 2,3-dihydro-1H-indolyl, C_3-C_6cycloalkenyl (wherein the cycloalkenyl contains one or two double bonds), thienyl, furyl, pyrrolyl, oxazolyl, imidazolyl, pyrazolyl, triazolyl, pyridyl, pyrimidyl, pyrazinyl and triazinyl.

Preferred R^6 substituents include hydrogen, C_1-C_3alkyl, cyclopropyl, cyclobutyl, cyclohexyl, C_1-C_3alkoxy, hydroxy and phenyl (wherein the phenyl is optionally substituted with one to two substituents independently selected from halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl or trifluoromethoxy); provided that R^6 is phenyl only when R^5 is phenyl.

Preferred R^8 substituents include hydrogen and C_1-C_3alkyl.

Preferably Z is selected from the group consisting of SO_2, C(=O) and –C(=O)-NH-.

Preferred  substituents include phenyl, naphthyl, quinolinyl and thienyl.

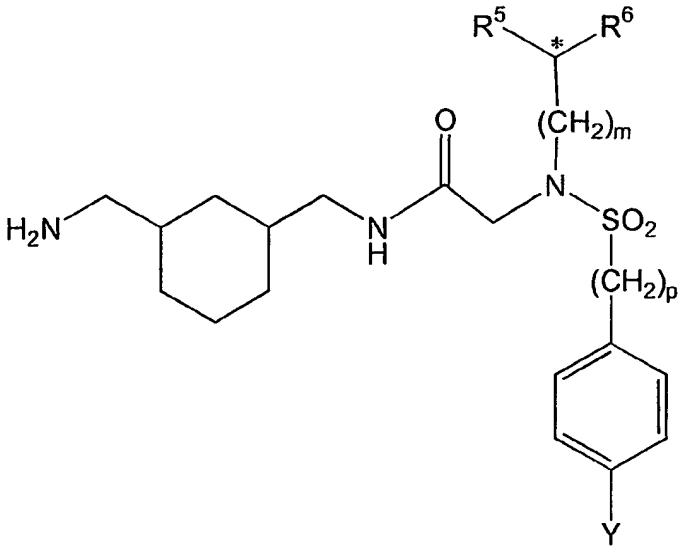
Preferably n is 0 to 2.

Preferred X substituents include halogen, C_1-C_6alkyl, C_1-C_4alkoxy, trifluoromethyl, trifluoromethoxy, nitro, acetamido, amino, C_1-C_3alkylamino and di(C_1-C_3alkyl)amino.

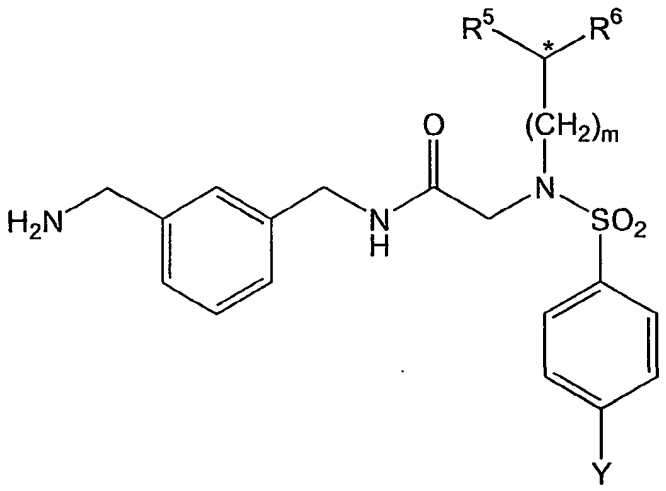
Preferred Y substituents include phenyl, naphthyl, (wherein the phenyl or naphthyl is optionally substituted with one to three substituents independently selected from halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl, trifluoromethoxy, formyl, nitro, cyano, methylthio, acetamido, amino, aminocarbonyl, C_1-C_3alkylamino, di(C_1-C_3alkyl)amino, carboxy, -COO(C_1-C_3alkyl), –COO(C_1-C_3alkylphenyl), C_1-$_4$alkylaminosulfonyl, C_1-C_4alkylcarbonylamino), biphenyl, 3,4-methylenedioxyphenyl, dianthryl, dibenzothienyl, phenoxathiinyl, a five membered heteroaryl (wherein the five membered heteroaryl contains one nitrogen, oxygen or sulfur atom and optionally contains an additional nitrogen or oxygen atom) and a six membered heteroaryl (wherein the six membered heteroaryl contains one nitrogen atom and optionally contains an additional nitrogen or oxygen atom); wherein the five or six membered heteroaryl is optionally substituted with one to two substituents independently selected from halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl, trifluoromethoxy, formyl, nitro, cyano, methylthio, acetamido, amino, aminocarbonyl, C_1-C_3alkylamino or di(C_1-C_3alkyl)amino; and wherein the point of attachment for the five or six membered heteroaryl is a carbon atom.

Particularly preferred compounds of the present invention are listed in Table 1, below.

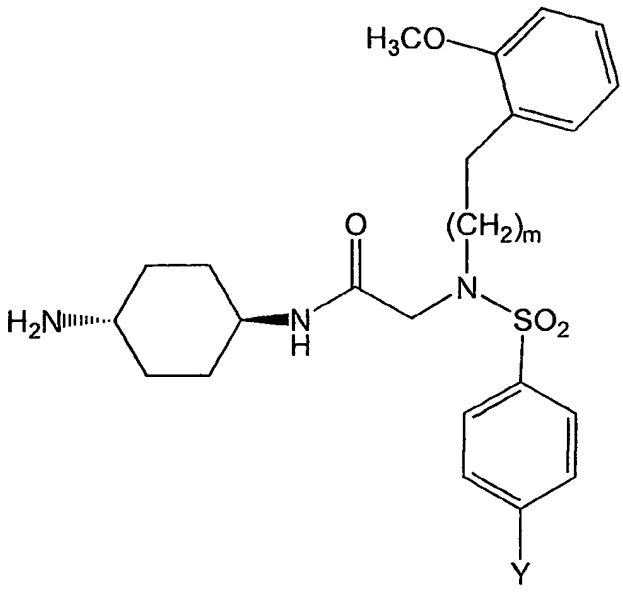
TABLE 1



Cmpd #	m	R^5	R^6	Stereo	p	Y
336	1	2-methoxyphenyl	H	-	0	2-methylphenyl
337	1	2-methoxyphenyl	H	-	0	2-chlorophenyl
338	1	2-methoxyphenyl	H	-	0	2-methoxyphenyl
339	1	2-methoxyphenyl	H	-	0	2,4-dichlorophenyl
340	0	2-methoxyphenyl	H	-	0	2-methylphenyl
341	0	2-methoxyphenyl	H	-	0	2-chlorophenyl
342	0	2-methoxyphenyl	H	-	0	2-methoxyphenyl
343	0	2-methoxyphenyl	H	-	0	2,4-dichlorophenyl
384	1	phenyl	CH_3	R	0	2-methylphenyl
385	1	phenyl	CH_3	R	0	2-chlorophenyl
386	1	phenyl	CH_3	R	0	3-fluorophenyl
387	1	phenyl	CH_3	S	0	2-methylphenyl
388	1	phenyl	CH_3	S	0	2-chlorophenyl
389	1	phenyl	CH_3	S	0	3-fluorophenyl

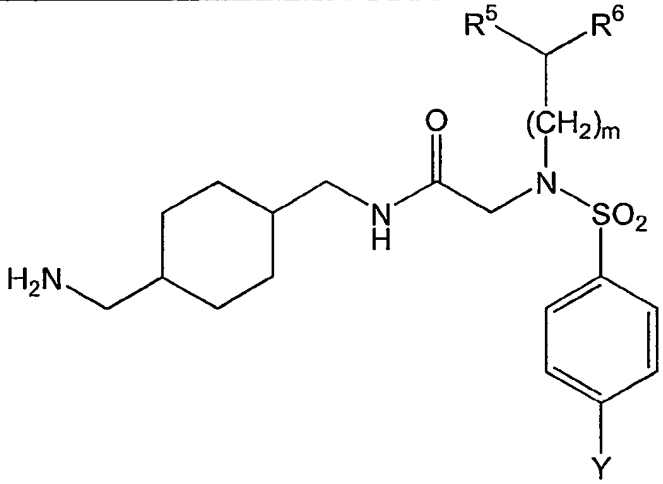


Cmpd #	m	R^5	R^6	Stereo	p	Y
344	1	2-methoxyphenyl	H	-	0	2-methylphenyl
345	1	2-methoxyphenyl	H	-	0	2-chlorophenyl
346	1	2-methoxyphenyl	H	-	0	2-methoxyphenyl
347	1	2-methoxyphenyl	H	-	0	2,4-dichlorophenyl
348	0	2-methoxyphenyl	H	-	0	2-methyl
349	0	2-methoxyphenyl	H	-	0	2-chlorophenyl
350	0	2-methoxyphenyl	H	-	0	2-methoxyphenyl
351	0	2-methoxyphenyl	H	-	0	2,4-dichlorophenyl
390	1	phenyl	CH_3	R	0	2-methylphenyl
391	1	phenyl	CH_3	R	0	2-chlorophenyl
392	1	phenyl	CH_3	R	0	3-fluorophenyl
393	1	phenyl	CH_3	S	0	2-methylphenyl
394	1	phenyl	CH_3	S	0	2-chlorophenyl
395	1	phenyl	CH_3	S	0	3-fluorophenyl



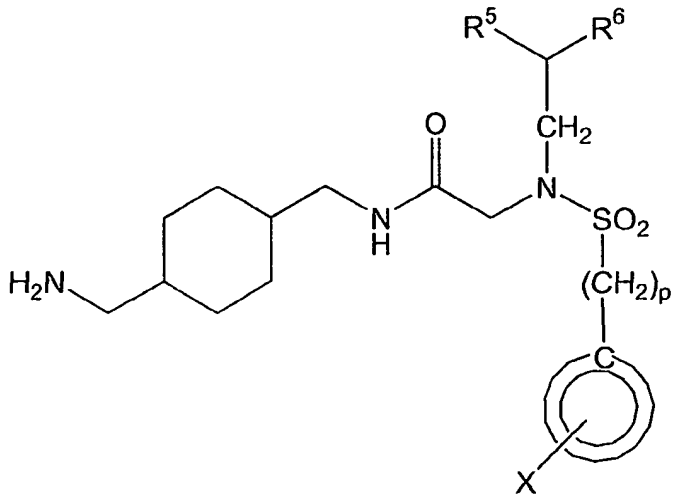
Cmpd #	m	Y
74	0	2-methylphenyl
75	0	3-thienyl
76	0	2-methoxyphenyl
77	0	4-fluorophenyl
78	0	2,3-dimethoxyphenyl
79	0	4-methoxyphenyl
80	0	4-methylphenyl
81	0	1-napthyl
82	0	2-chlorophenyl
83	0	3-pyridyl
84	0	2-thienyl
85	0	3-aminocarbonylphenyl
86	0	phenyl
87	0	4-chlorophenyl
88	0	4-[3,5-dimethylisoxazolyl]
89	0	2-furyl
90	0	4-cyanophenyl
91	0	4-pyridyl
92	0	3-methoxyphenyl
93	0	4-aminophenyl

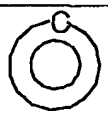
94	1	2-methylphenyl
95	1	3-thienyl
96	1	2-methoxyphenyl
97	1	4-fluorophenyl
98	1	2,3-dimethyoxyphenyl
99	1	4-methoxyphenyl
100	1	4-methylphenyl
101	1	1-napthyl
102	1	2-chlorophenyl
103	1	3-pyridyl
104	1	2-thienyl
105	1	3-aminocarbonylphenyl
106	1	phenyl
107	1	4-chlorophenyl
108	1	4-[3,4-dimethylisoxazolyl]
109	1	2-furyl
110	1	4-cyano phenyl
111	1	4-pyridyl
112	1	3-methoxyphenyl
113	1	4-aminophenyl



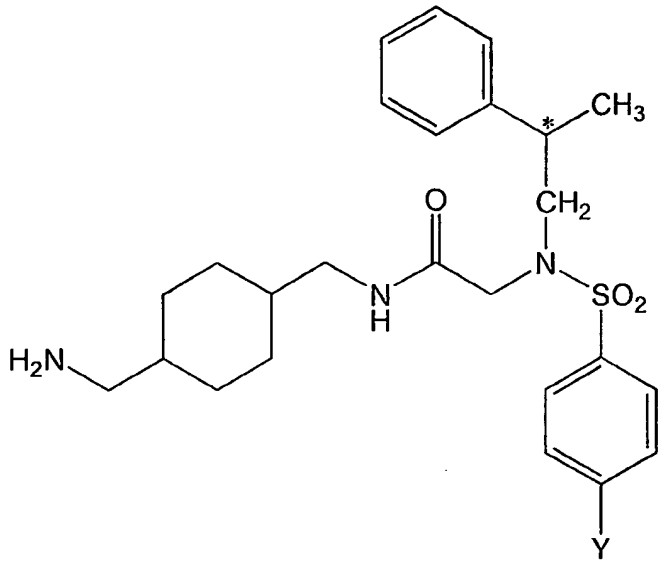
Cmpd #	m	R^5	R^6	Y
1	0	2-methoxyphenyl	H	4-chlorophenyl
2	0	2-methoxyphenyl	H	3-trifluoromethylphenyl

3	0	2-methoxyphenyl	H	2-chlorophenyl
4	0	2-methoxyphenyl	H	2-methylphenyl
5	0	2-methoxyphenyl	H	2-methoxyphenyl
6	0	2-methoxyphenyl	H	2,4-dichlorophenyl
7	0	2-methoxyphenyl	H	3,5-di(trifluoromethyl) phenyl
8	0	2-methoxyphenyl	H	3-chloro-4-fluorophenyl
9	0	2-methoxyphenyl	H	4-methoxyphenyl
20	0	3-methoxyphenyl	H	3-trifluoromethylphenyl
21	0	3-methoxyphenyl	H	2-methoxyphenyl
22	0	3-methoxyphenyl	H	2,4-dichlorophenyl
23	0	3-methoxyphenyl	H	3-fluorophenyl
24	0	3-methoxyphenyl	H	3-methoxyphenyl
25	0	3-methoxyphenyl	H	4-methylphenyl
26	0	3-methoxyphenyl	H	4-fluorophenyl
27	0	3-methoxyphenyl	H	3-chloro-4-fluorophenyl
28	0	3-methoxyphenyl	H	4-methoxyphenyl
29	1	2-methoxyphenyl	H	3-trifluoromethyl phenyl
30	1	2-methoxyphenyl	H	3-nitrophenyl
31	1	2-methoxyphenyl	H	2-chlorophenyl
32	1	2-methoxyphenyl	H	2-methylphenyl
33	1	2-methoxyphenyl	H	2-methoxyphenyl
34	1	2-methoxyphenyl	H	2,4-dichlorophenyl
35	1	2-methoxyphenyl	H	phenyl
36	1	2-methoxyphenyl	H	3-chlorophenyl
37	1	2-methoxyphenyl	H	4-fluorophenyl
38	1	2-methoxyphenyl	H	2-trifluoromethyl phenyl

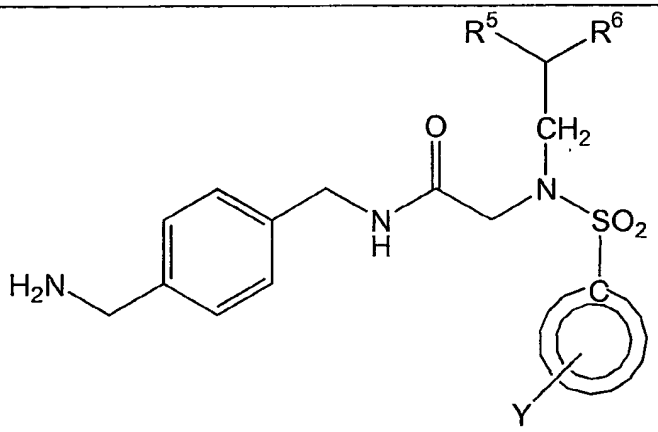


Cmpd #	R^5	R^6	p		X
39	2-methoxyphenyl	H	0	phenyl	-
40	2-methoxyphenyl	H	0	2-thienyl	5-chloro
41	2-methoxyphenyl	H	0	1-phenyl	3-trifluoromethyl
42	2-methoxyphenyl	H	0	1-phenyl	2-trifluoromethyl
43	2-methoxyphenyl	H	0	1-phenyl	3-chloro
44	2-methoxyphenyl	H	0	1-phenyl	3,4-dichloro
45	2-methoxyphenyl	H	0	2-napthyl	-
46	2-methoxyphenyl	H	0	1-phenyl	2-chloro
47	2-methoxyphenyl	H	0	1-phenyl	4-chloro
48	2-methoxyphenyl	H	0	3-thienyl	2,5-dichloro
49	2-methoxyphenyl	H	0	1-phenyl	2,4-dichloro
50	2-methoxyphenyl	H	0	1-phenyl	2,6-dichloro
51	2-methoxyphenyl	H	0	1-phenyl	3,5-dichloro
52	2-methoxyphenyl	H	0	1-phenyl	2,5-dichloro
53	2-methoxyphenyl	H	0	1-phenyl	2,3-dichloro
54	2-methoxyphenyl	H	1	phenyl	-
55	2-methoxyphenyl	H	0	1-phenyl	4-methyl

56	2-methoxyphenyl	H	0	1-phenyl	4-methoxy
57	2-methoxyphenyl	H	0	1-napthyl	-
58	2-methoxyphenyl	H	0	1-phenyl	4-fluoro
59	2-methoxyphenyl	H	0	1-phenyl	3,4-dimethoxy
60	2-methoxyphenyl	H	0	1-phenyl	2,5-dimethoxy
61	2-methoxyphenyl	H	0	1-phenyl	2-nitro
62	2-methoxyphenyl	H	0	1-phenyl	4-nitro
63	2-methoxyphenyl	H	0	1-phenyl	3-nitro
64	2-methoxyphenyl	H	0	1-phenyl	4-iodo
65	2-methoxyphenyl	H	0	1-phenyl	4-tert-butyl
66	2-methoxyphenyl	H	0	1-phenyl	2-nitro-4-methoxy
67	2-methoxyphenyl	H	0	1-phenyl	3-methyl-4-methoxy
68	2-methoxyphenyl	H	0	1-phenyl	2-nitro-4-trifluoromethyl
69	2-methoxyphenyl	H	0	1-phenyl	3-fluoro
70	2-methoxyphenyl	H	0	1-phenyl	2-fluoro
71	2-methoxyphenyl	H	0	1-phenyl	4-trifluoromethyl
72	2-methoxyphenyl	H	0	1-phenyl	4-trifluoromethoxy
402	2-methoxyphenyl	H	0	1-phenyl	2,3-dichloro
403	3,4-methylene dioxyphenyl	H	0	8-quinolinyl	-



Cmpd #	Stereo	Y
372	R	2-methylphenyl
373	R	2-chlorophenyl
374	R	3-fluorophenyl
375	S	2-methylphenyl
376	S	2-chlorophenyl
377	S	3-fluorophenyl



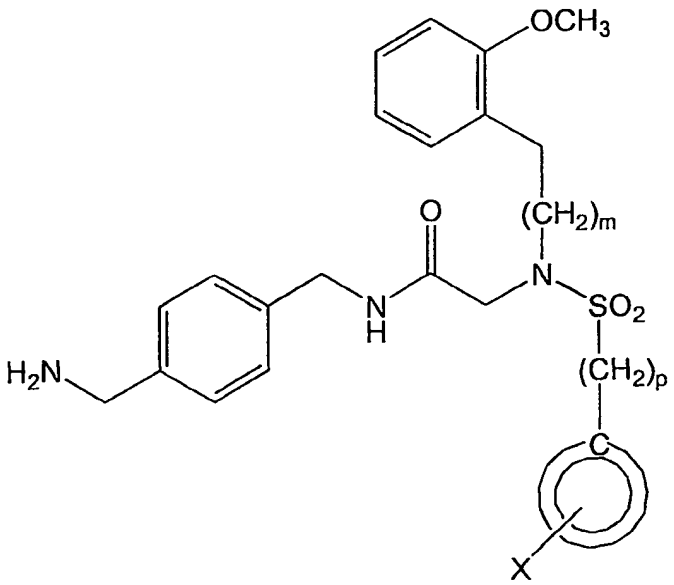
Cmpd #	R^5	R^6	Stereo	C	Y
10	2-methoxyphenyl	H	-	1,4-phenyl	3-nitrophenyl
11	2-methoxyphenyl	H	-	1,4-phenyl	2-chlorophenyl
12	2-methoxypphenyl	H	-	1,4-phenyl	2-methylphenyl

13	2-methoxyphenyl	H	-	1,4-phenyl	2-methoxy phenyl
14	2-methoxyphenyl	H	-	1,4-phenyl	3-fluorophenyl
15	2-methoxyphenyl	H	-	1,4-phenyl	phenyl
16	2-methoxyphenyl	H	-	1,4-phenyl	3-methoxy phenyl
17	2-methoxyphenyl	H	-	1,4-phenyl	4-fluorophenyl
18	2-methoxyphenyl	H	-	1,4-phenyl	2-trifluoro methylphenyl
19	2-methoxyphenyl	H	-	1,4-phenyl	3-chloro-4-fluorophenyl
197	phenyl	H	R	1,4-phenyl	phenyl
207	phenyl	H	S	1,4-phenyl	phenyl
208	phenyl	H	S	1,4-phenyl	2-chlorophenyl
209	phenyl	H	S	1,4-phenyl	3-chlorophenyl
210	phenyl	H	S	1,4-phenyl	2-methoxyphenyl
211	phenyl	H	S	1,4-phenyl	3-methoxyphenyl
212	phenyl	H	S	1,4-phenyl	4-methoxyphenyl
213	phenyl	H	S	1,4-phenyl	3-fluorophenyl
214	phenyl	H	S	1,4-phenyl	4-fluorophenyl
215	phenyl	H	S	1,4-phenyl	2-methylphenyl
216	phenyl	H	S	1,4-phenyl	4-methylphenyl
217	2-methoxyphenyl	H	-	1,2-phenyl	2-thienyl
218	2-methoxyphenyl	H	-	1,2-phenyl	2-methylphenyl
219	2-methoxyphenyl	H	-	1,2-phenyl	3-thienyl
220	2-methoxyphenyl	H	-	1,2-phenyl	2-methoxyphenyl
221	2-methoxyphenyl	H	-	1,2-phenyl	4-fluorophenyl
222	2-methoxyphenyl	H	-	1,2-phenyl	4-methoxyphenyl
223	2-methoxyphenyl	H	-	1,2-phenyl	4-methylphenyl
224	2-methoxyphenyl	H	-	1,2-phenyl	1-napthyl
225	2-methoxyphenyl	H	-	1,2-phenyl	4-chlorophenyl
226	2-methoxyphenyl	H	-	1,2-phenyl	3-methoxy phenyl

227	2-methoxyphenyl	H	-	1,2-phenyl	3-aminophenyl
228	2-methoxyphenyl	H	-	1,2-phenyl	3-fluorophenyl
229	2-methoxyphenyl	H	-	1,2-phenyl	2-fluorophenyl
230	2-methoxyphenyl	H	-	1,2-phenyl	1-(3,4-methylene dioxyphenyl)
232	2-methoxyphenyl	H	-	1,2-phenyl	phenyl
233	2-methoxyphenyl	H	-	1,2-phenyl	4-(3,5-dimethyl isoxazole)
234	2-methoxyphenyl	H	-	1,2-phenyl	4-cyanophenyl
235	2-methoxyphenyl	H	-	1,2-phenyl	4-pyridyl
236	2-methoxyphenyl	H	-	1,2-phenyl	2,3,4-trimethoxyphenyl
237	2-methoxyphenyl	H	-	1,2-phenyl	3-cyanophenyl
238	2-methoxyphenyl	H	-	1,2-phenyl	2,5-dimethoxy phenyl
239	2-methoxyphenyl	H	-	1,2-phenyl	2,4-dichloro phenyl
240	2-methoxyphenyl	H	-	1,2-phenyl	3-trifluoro methylphenyl
241	2-methoxyphenyl	H	-	1,2-phenyl	4-trifluoro methylphenyl
242	2-methoxyphenyl	H	-	1,2-phenyl	2-trifluoro methylphenyl
243	2-methoxyphenyl	H	-	1,2-phenyl	3-methylphenyl
244	2-methoxyphenyl	H	-	1,3-phenyl	2-methylphenyl
245	2-methoxyphenyl	H	-	1,3-phenyl	3-thienyl
246	2-methoxyphenyl	H	-	1,3-phenyl	2-methoxyphenyl
247	2-methoxyphenyl	H	-	1,3-phenyl	4-fluorophenyl
248	2-methoxyphenyl	H	-	1,3-phenyl	4-methoxyphenyl
249	2-methoxyphenyl	H	-	1,3-phenyl	4-methoxyphenyl
250	2-methoxyphenyl	H	-	1,3-phenyl	1-napthyl
252	2-methoxyphenyl	H	-	1,3-phenyl	3-pyridyl
253	2-methoxyphenyl	H	-	1,3-phenyl	4-chlorophenyl

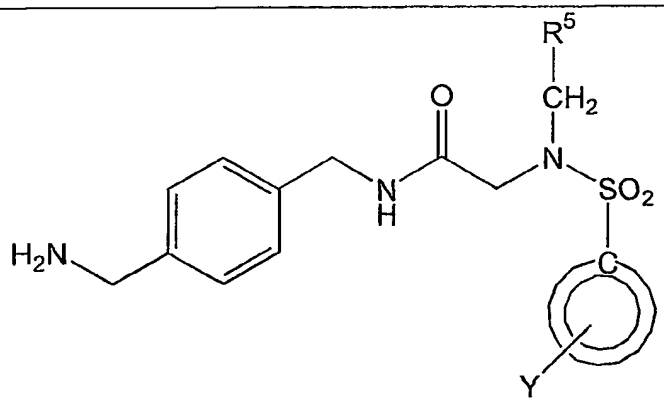
254	2-methoxyphenyl	H	-	1,3-phenyl	3-methoxyphenyl
255	2-methoxyphenyl	H	-	1,3-phenyl	3-aminophenyl
256	2-methoxyphenyl	H	-	1,3-phenyl	3-fluorophenyl
257	2-methoxyphenyl	H	-	1,3-phenyl	2-fluorophenyl
258	2-methoxyphenyl	H	-	1,3-phenyl	1-(3,4-methylene dioxyphenyl)
259	2-methoxyphenyl	H	-	1,3-phenyl	3-chlorophenyl
260	2-methoxyphenyl	H	-	1,3-phenyl	phenyl
261	2-methoxyphenyl	H	-	1,3-phenyl	4-(3,5-dimethyl isoxazole)
262	2-methoxyphenyl	H	-	1,3-phenyl	4-cyanophenyl
263	2-methoxyphenyl	H	-	1,3-phenyl	4-pyridyl
264	2-methoxyphenyl	H	-	1,3-phenyl	2,3,4-trimethoxyphenyl
265	2-methoxyphenyl	H	-	1,3-phenyl	4-cyanophenyl
266	2-methoxyphenyl	H	-	1,3-phenyl	2,5-dimethoxy phenyl
267	2-methoxyphenyl	H	-	1,3-phenyl	3-trifluoro methylphenyl
268	2-methoxyphenyl	H	-	1,3-phenyl	4-trifluoro methylphenyl
269	2-methoxyphenyl	H	-	1,3-phenyl	2-trifluoro methylphenyl
270	2-methoxyphenyl	H	-	1,3-phenyl	3-methylphenyl
271	2-methoxyphenyl	H	-	2,5-thienyl	2-thienyl
272	2-methoxyphenyl	H	-	2,5-thienyl	2-methylphenyl
273	2-methoxyphenyl	H	-	2,5-thienyl	3-thienyl
274	2-methoxyphenyl	H	-	2,5-thienyl	2-methoxyphenyl
275	2-methoxyphenyl	H	-	2,5-thienyl	4-fluorophenyl
276	2-methoxyphenyl	H	-	2,5-thienyl	4-methoxyphenyl
277	2-methoxyphenyl	H	-	2,5-thienyl	4-methylphenyl
279	2-methoxyphenyl	H	-	2,5-thienyl	2-chlorophenyl
280	2-methoxyphenyl	H	-	2,5-thienyl	3-pyridyl

281	2-methoxyphenyl	H	-	2,5-thienyl	4-chlorophenyl
282	2-methoxyphenyl	H	-	2,5-thienyl	3-methoxyphenyl
283	2-methoxyphenyl	H	-	2,5-thienyl	3-aminophenyl
284	2-methoxyphenyl	H	-	2,5-thienyl	3-fluorophenyl
285	2-methoxyphenyl	H	-	2,5-thienyl	2-fluorophenyl
287	2-methoxyphenyl	H	-	2,5-thienyl	3-chlorophenyl
288	2-methoxyphenyl	H	-	2,5-thienyl	phenyl
289	2-methoxyphenyl	H	-	2,5-thienyl	4-(3,5-dimethyl isoxazole)
290	2-methoxyphenyl	H	-	2,5-thienyl	4-cyanophenyl
291	2-methoxyphenyl	H	-	2,5-thienyl	4-pyridyl
292	2-methoxyphenyl	H	-	2,5-thienyl	2,3,4,-trimethoxyphenyl
293	2-methoxyphenyl	H	-	2,5-thienyl	3-cyanophenyl
294	2-methoxyphenyl	H	-	2,5-thienyl	2-furyl
295	2-methoxyphenyl	H	-	2,5-thienyl	2,5-dimethoxy phenyl
296	2-methoxyphenyl	H	-	2,5-thienyl	2,4-dichloro phenyl
297	2-methoxyphenyl	H	-	2,5-thienyl	3-trifluoro methylphenyl
298	2-methoxyphenyl	H	-	2,5-thienyl	4-trifluoro methylphenyl
299	2-methoxyphenyl	H	-	2,5-thienyl	2-trifluoro methylphenyl
300	2-methoxyphenyl	H	-	2,5-thienyl	3-methylphenyl

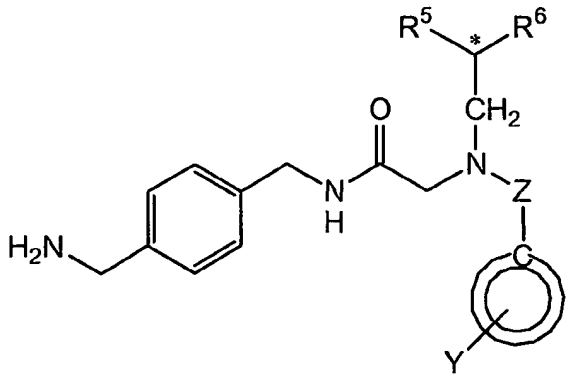


Cmpd #	p	m	C 	X
114	0	1	2-thienyl	5-chloro
115	0	1	phenyl	3-trifluoromethyl
116	0	1	phenyl	2-trifluoromethyl
117	0	1	phenyl	3-chloro
118	0	1	phenyl	3,4-dichloro
119	0	1	2-napthyl	-
120	0	1	phenyl	2-chloro
121	0	1	phenyl	2,5-dimethoxy
122	0	1	phenyl	2,4-dichloro
123	0	1	phenyl	2,6-dichloro
124	0	1	phenyl	2,5-dichloro
125	0	1	phenyl	3,5-dichloro
126	0	1	2-thienyl	4,5-dichloro
127	1	1	phenyl	-
128	0	1	phenyl	4-methoxy
129	0	1	1-napthyl	-
130	0	1	phenyl	4-fluoro
131	0	1	phenyl	3-fluoro
132	0	1	phenyl	2-fluoro

133	0	1	phenyl	3,4-dimethoxy
134	0	1	phenyl	2-nitro
135	0	1	phenyl	3-nitro
136	0	1	phenyl	4-nitro
137	0	1	phenyl	4-iodo
138	0	1	phenyl	4-t-butyl
139	0	1	phenyl	2-nitro-4-methoxy
140	0	1	phenyl	2-methoxy-5-methyl
141	0	1	2-thienyl	4-nitro-5-chloro
142	0	1	phenyl	2-nitro-4-trifluoro methyl
143	0	1	phenyl	4-trifluoromethyl
144	0	1	phenyl	4-trifluoromethoxy
147	0	1	2-thienyl	-
148	0	1	phenyl	4-methyl
149	0	1	phenyl	4-chloro
150	0	1	phenyl	-
404	0	0	1-phenyl	2,3-dichloro



Cmpd #	R^5	C	Y
73	2-methoxyphenyl	2,-thienyl	5-(2-methylthio-pyrimidyl)
405	3,4-methylene dioxyphenyl	8-quinolinyl	-



Cmpd #	R^5	R^6	Stereo	Z	C	Y
145	2-methoxy phenyl	H	-	SO_2	2,5-thienyl	2-pyridyl
146	2-methoxy phenyl	H	-	SO_2	2,5-thienyl	5-(2-methylthio-pyrimidyl)
198	phenyl	CH_3	R	SO_2	1,4-phenyl	2-chlorophenyl
199	phenyl	CH_3	R	SO_2	1,4-phenyl	3-chlorophenyl
200	phenyl	CH_3	R	SO_2	1,4-phenyl	2-methoxyphenyl
201	phenyl	CH_3	R	SO_2	1,4-phenyl	3-methoxyphenyl
202	phenyl	CH_3	R	SO_2	1,4-phenyl	4-methoxyphenyl
203	phenyl	CH_3	R	SO_2	1,4-phenyl	3-fluorophenyl
204	phenyl	CH_3	R	SO_2	1,4-phenyl	4-fluorophenyl
205	phenyl	CH_3	R	SO_2	1,4-phenyl	2-methylphenyl
206	phenyl	CH_3	R	SO_2	1,4-phenyl	4-methylphenyl
231	2-methoxy phenyl	H	-	SO_2	1,2-phenyl	3-chlorophenyl
251	2-methoxy phenyl	H	-	SO_2	1,3-phenyl	2-chlorophenyl
278	2-methoxy phenyl	H	-	SO_2	2,5-thienyl	1-naphthyl
286	2-methoxy phenyl	H	-	SO_2	2,5-thienyl	1-(3,4-methylene dioxyphenyl)
301	phenyl	CH_3	R	SO_2	1,4-phenyl	2-fluorophenyl
302	phenyl	CH_3	R	SO_2	1,4-phenyl	2,6-dichlorophenyl

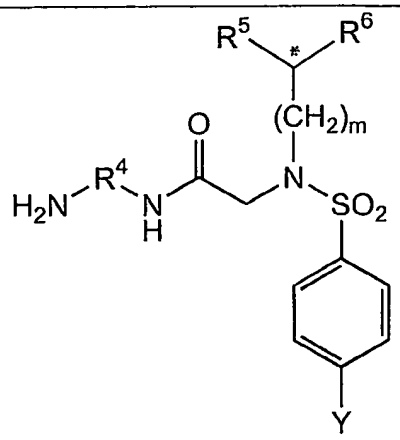
303	phenyl	CH_3	R	SO_2	1,4-phenyl	2,4-dichlorophenyl
304	phenyl	CH_3	R	SO_2	1,4-phenyl	2-trifluoromethyl phenyl
305	phenyl	CH_3	R	SO_2	1,4-phenyl	2,4,6-trimethyl phenyl
306	phenyl	CH_3	S	SO_2	1,4-phenyl	2-fluorophenyl
307	phenyl	CH_3	S	SO_2	1,4-phenyl	2,6-difluorophenyl
308	phenyl	CH_3	S	SO_2	1,4-phenyl	2,4-dichlorophenyl
309	phenyl	CH_3	S	SO_2	1,4-phenyl	2-trifluoromethyl phenyl
310	phenyl	CH_3	S	SO_2	1,4-phenyl	2,4,6-trimethylphenyl
311	phenyl	CH_3	Mix	SO_2	1,4-phenyl	2-methylphenyl
312	phenyl	CH_3	Mix	SO_2	1,4-phenyl	2-chlorophenyl
313	phenyl	CH_3	Mix	SO_2	1,4-phenyl	3-fluorophenyl
314	4-chloro phenyl	CH_3	Mix	SO_2	1,4-phenyl	2-methylphenyl
315	4-chloro phenyl	CH_3	Mix	SO_2	1,4-phenyl	2-chlorophenyl
316	4-chloro phenyl	CH_3	Mix	SO_2	1,4-phenyl	3-fluorophenyl
317	4-chloro phenyl	cyclo-propyl	-	SO_2	1,4-phenyl	2-methylphenyl
318	4-chloro phenyl	cyclo-propyl	-	SO_2	1,4-phenyl	2-chlorophenyl
319	4-chloro phenyl	cyclo-propyl	-	SO_2	1,4-phenyl	3-fluorophenyl
323	phenyl	H	-	SO_2	1,4-phenyl	2-methylphenyl
324	phenyl	H	-	SO_2	1,4-phenyl	2-chlorophenyl
325	phenyl	H	-	SO_2	1,4-phenyl	3-fluorophenyl
412	phenyl	CH_3	R	SO_2	1,4-phenyl	phenyl
413	phenyl	CH_3	R	SO_2	1,4-phenyl	3-nitrophenyl
414	phenyl	CH_3	R	SO_2	1,4-phenyl	4-fluorophenyl

415	phenyl	CH_3	R	SO_2	1,4-phenyl	2-methylphenyl
416	phenyl	CH_3	R	SO_2	1,4-phenyl	3-trifluoromethyl phenyl
417	phenyl	CH_3	R	SO_2	1,4-phenyl	4-trifluoromethyl phenyl
418	phenyl	CH_3	R	SO_2	1,4-phenyl	3-chlorophenyl
419	phenyl	CH_3	R	SO_2	1,4-phenyl	3-methoxy phenyl
420	phenyl	CH_3	R	SO_2	1,4-phenyl	2-trifluoromethyl phenyl
421	phenyl	CH_3	R	SO_2	1,4-phenyl	2-methoxy phenyl
422	phenyl	CH_3	R	SO_2	1,4-phenyl	4-trifluoro methoxyphenyl
423	phenyl	CH_3	R	SO_2	1,4-phenyl	3-fluorophenyl
424	phenyl	CH_3	R	SO_2	1,4-phenyl	2-naphthyl
425	phenyl	CH_3	R	SO_2	1,4-phenyl	3-chloro-4-fluorophenyl
426	phenyl	CH_3	R	SO_2	1,4-phenyl	3-bromophenyl
427	phenyl	CH_3	R	SO_2	1,4-phenyl	4-chlorophenyl
428	phenyl	CH_3	R	SO_2	1,4-phenyl	3,5-dichloro phenyl
429	phenyl	CH_3	R	SO_2	1,4-phenyl	2,4-dichloro phenyl
430	phenyl	CH_3	R	SO_2	1,4-phenyl	3,5-ditrifluoro methylphenyl
432	phenyl	CH_3	R	SO_2	1,4-phenyl	2-benzofuryl
433	phenyl	CH_3	R	SO_2	1,4-phenyl	2-(t-butylamino sulfonyl)phenyl
434	phenyl	CH_3	R	SO_2	1,4-phenyl	4-cyanophenyl
435	phenyl	CH_3	R	SO_2	1,4-phenyl	3-cyanophenyl
436	phenyl	CH_3	R	SO_2	1,4-phenyl	3-carboxyphenyl
437	phenyl	CH_3	R	SO_2	1,4-phenyl	2[(di-i-propyl) aminocarbonyl] phenyl

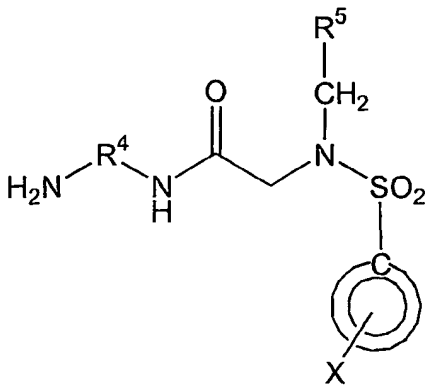
438	phenyl	CH_3	R	SO_2	1,4-phenyl	4-(3,5-dimethyl) isoxazolyl
439	phenyl	CH_3	R	SO_2	1,4-phenyl	2-methoxy-5-formylphenyl
440	phenyl	CH_3	R	SO_2	1,4-phenyl	4-pyridyl
441	phenyl	CH_3	R	SO_2	1,4-phenyl	2,3,4-tri methoxyphenyl
442	phenyl	CH_3	R	SO_2	1,4-phenyl	phenoxathiinyl
443	phenyl	CH_3	R	SO_2	1,4-phenyl	2-(5-formyl)furyl
444	phenyl	CH_3	R	SO_2	1,4-phenyl	2-(4-methyl) thienyl
446	phenyl	CH_3	R	SO_2	1,4-phenyl	dibenzothienyl
447	phenyl	CH_3	R	SO_2	1,4-phenyl	dianthrenyl
448	phenyl	CH_3	R	SO_2	1,4-phenyl	dibenzothienyl
449	phenyl	CH_3	R	SO_2	1,4-phenyl	3-benzothienyl
450	phenyl	CH_3	R	SO_2	1,4-phenyl	3,4-dimethoxy phenyl
451	phenyl	CH_3	R	SO_2	1,4-phenyl	2-fluorophenyl
452	phenyl	CH_3	R	SO_2	1,4-phenyl	1-naphthyl
453	phenyl	CH_3	R	SO_2	1,4-phenyl	4-methoxy phenyl
454	phenyl	CH_3	R	SO_2	1,4-phenyl	3-fluoro-4-chlorophenyl
455	phenyl	CH_3	R	SO_2	1,4-phenyl	2-nitrophenyl
456	phenyl	CH_3	R	SO_2	1,4-phenyl	3-biphenyl
457	phenyl	CH_3	R	SO_2	1,4-phenyl	2-(t-butylcarbonyl amino)-3-methoxy phenyl
458	phenyl	CH_3	R	SO_2	1,4-phenyl	2-(t-butyl carbonyl amino)-5-methoxy phenyl
459	phenyl	CH_3	R	SO_2	1,4-phenyl	2-(5-formyl)furyl
460	phenyl	CH_3	R	SO_2	1,4-phenyl	2,5-dimethoxy phenyl

461	phenyl	CH_3	R	SO_2	1,4-phenyl	2-(di(i-propyl) aminocarbonyl)-3-methoxyphenyl
462	phenyl	CH_3	R	SO_2	1,4-phenyl	4-methylthio phenyl
463	phenyl	CH_3	R	SO_2	1,4-phenyl	2,4,6-tri methylphenyl
464	phenyl	CH_3	R	SO_2	1,4-phenyl	3-methylphenyl
465	phenyl	CH_3	R	SO_2	1,4-phenyl	4-methylphenyl
466	phenyl	CH_3	R	SO_2	1,4-phenyl	3-pyridyl
467	phenyl	CH_3	R	SO_2	1,4-phenyl	3-aminophenyl
468	phenyl	CH_3	R	SO_2	1,4-phenyl	3-methylcarbonyl aminophenyl
477	phenyl	CH_3	R	C(O)	1,4-phenyl	2-chlorophenyl
478	phenyl	CH_3	R	C(O)	1,4-phenyl	2-methylphenyl
479	phenyl	CH_3	R	C(O)	1,4-phenyl	3-fluorophenyl
480	phenyl	CH_3	R	C(O)	1,4-phenyl	2-bromophenyl
481	phenyl	CH_3	R	C(O)	1,4-phenyl	2,5-dichloro phenyl
521	phenyl	CH_3	R	SO_2	1,4-phenyl	2-methyl-3-chlorophenyl
522	phenyl	CH_3	R	SO_2	1,4-phenyl	2-chloro-5-methylphenyl
523	phenyl	CH_3	R	SO_2	1,4-phenyl	2-methyl-5-chlorophenyl
524	phenyl	CH_3	R	SO_2	1,4-phenyl	3-chloro-4-methylphenyl
525	phenyl	CH_3	R	SO_2	1,4-phenyl	2-chloro-6-methylphenyl
526	phenyl	CH_3	R	SO_2	1,4-phenyl	2-chloro-4-methylphenyl
550	3-trifluoro methyl	H	-	SO_2	1,4-phenyl	phenyl

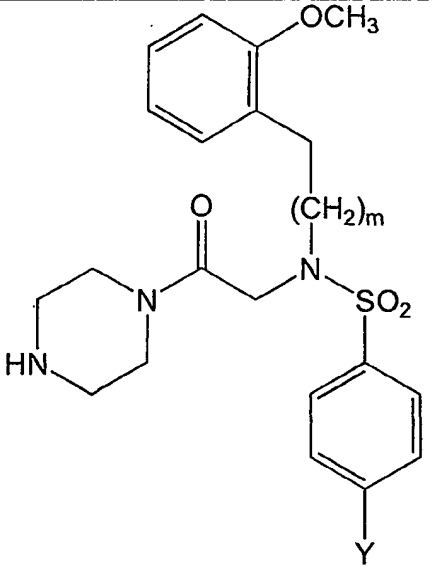
	phenyl					
590	phenyl	CH_3	R	C(O)NH	1,4-phenyl	phenyl
591	phenyl	CH_3	S	C(O)NH	1,4-phenyl	phenyl



Cmpd #	R^4	m	R^5	R^6	Stereo	Y
378	1,5-n-pentyl	1	phenyl	CH_3	R	2-methylphenyl
379	1,5-n-pentyl	1	phenyl	CH_3	R	2-chlorophenyl
380	1,5-n-pentyl	1	phenyl	CH_3	R	3-fluorophenyl
381	1,5-n-pentyl	1	phenyl	CH_3	S	2-methylphenyl
382	1,5-n-pentyl	1	phenyl	CH_3	S	2-chlorophenyl
383	1,5-n-pentyl	1	phenyl	CH_3	S	3-fluorophenyl
352	1,5-n-pentyl	1	2-methoxyphenyl	H	-	2-methylphenyl
353	1,6-n-hexyl	1	2-methoxyphenyl	H	-	2-chlorophenyl
354	1,6-n-hexyl	1	2-methoxyphenyl	H	-	2-methoxyphenyl
355	1,6-n-hexyl	1	2-methoxyphenyl	H	-	2,4-dichlorophenyl
356	1,6-n-hexyl	0	2-methoxyphenyl	H	-	2-methylphenyl
357	1,6-n-hexyl	0	2-methoxyphenyl	H	-	2-chlorophenyl
358	1,6-n-hexyl	0	2-methoxyphenyl	H	-	2-methoxyphenyl
359	1,6-n-hexyl	0	2-methoxyphenyl	H	-	2,4-dichlorophenyl
396	1,6-n-hexyl	1	phenyl	CH_3	R	2-methylphenyl
397	1,6-n-hexyl	1	phenyl	CH_3	R	2-chlorophenyl
398	1,6-n-hexyl	1	phenyl	CH_3	R	3-fluorophenyl
399	1,6-n-hexyl	1	phenyl	CH_3	S	2-methylphenyl
400	1,6-n-hexyl	1	phenyl	CH_3	S	2-chlorophenyl
401	1,6-n-hexyl	1	phenyl	CH_3	S	3-fluorophenyl



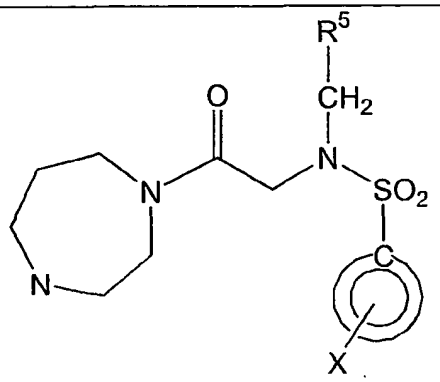
Cmpd #	R^4	R^5	C	X
406	1,4-n-butyl	2-methoxyphenyl	1-phenyl	2,3-dichloro
407	1,6-n-hexyl	2-methoxyphenyl	1-phenyl	2,3-dichloro
408	1,4-n-butyl	3,4-methylene dioxyphenyl	8-quinolinyl	-
409	1,6-n-hexyl	3,4-methylene dioxyphenyl	8-quinolinyl	-



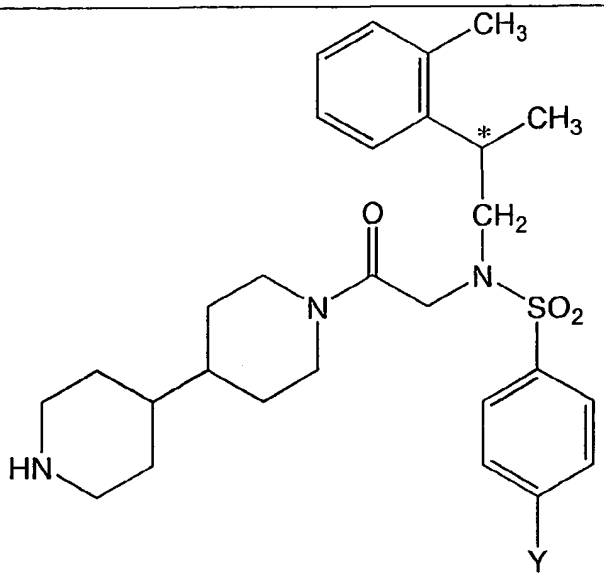
Cmpd #	m	Y
151	1	2-methylphenyl
152	1	3-thienyl
153	1	2-methoxyphenyl
154	1	4-fluorophenyl

155	1	2,4-dimethoxyphenyl
156	1	4-methoxyphenyl
157	1	4-methylphenyl
158	1	1-napthyl
159	1	2-chlorophenyl
160	1	3-pyridyl
161	1	2-thienyl
162	1	3-acetamidophenyl
163	1	phenyl
164	1	4-chlorophenyl
165	1	4-[3,5-dimethylisoxazolyl]
166	1	3-chlorophenyl
167	1	4-cyanophenyl
168	1	4-pyridyl
169	1	3-methoxyphenyl
170	1	3-aminophenyl
171	1	3-fluorophenyl
172	1	2-fluorophenyl
173	1	3,4-methylenedioxyphenyl
174	0	2-methylphenyl
175	0	3-thienyl
176	0	2-methoxyphenyl
177	0	4-fluorophenyl
178	0	2,4-dimethoxyphenyl
179	0	4-methoxyphenyl
180	0	4-methylphenyl
181	0	1-napthyl
182	0	2-chlorophenyl
183	0	3-pyridyl
184	0	2-thienyl
185	0	3-acetamidophenyl
186	0	phenyl
187	0	4-chlorophenyl

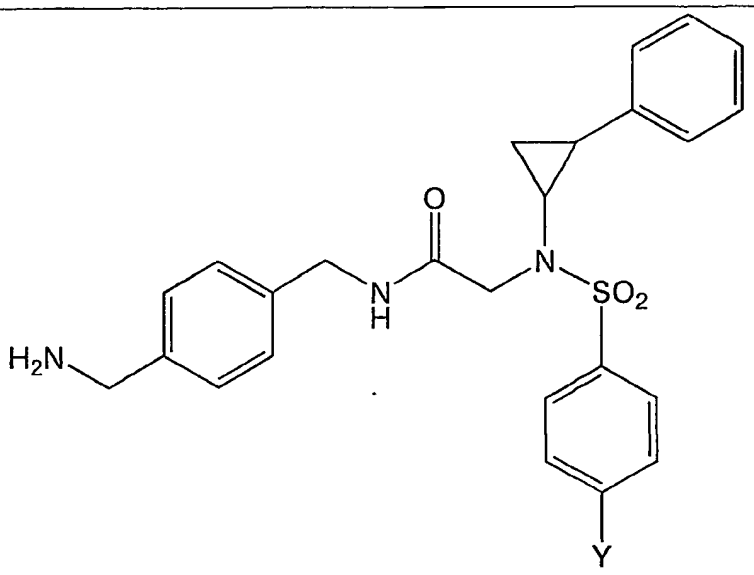
188	0	4-[3,5-dimethylisoxazolyl]
189	0	3-chlorophenyl
190	0	4-cyanophenyl
191	0	4-pyridyl
192	0	3-methoxyphenyl
193	0	3-aminophenyl
194	0	3-fluorophenyl
195	0	2-fluorophenyl
196	0	3,4-methylenedioxyphenyl



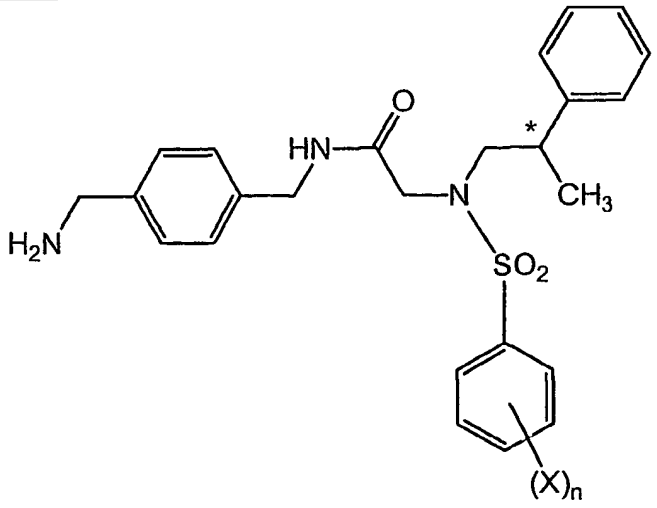
Cmpd #	R^5	C	X
410	2-methoxyphenyl	1-phenyl	2,3-dichloro
411	3,4-methylenedioxyphenyl	8-quinolinyl	-



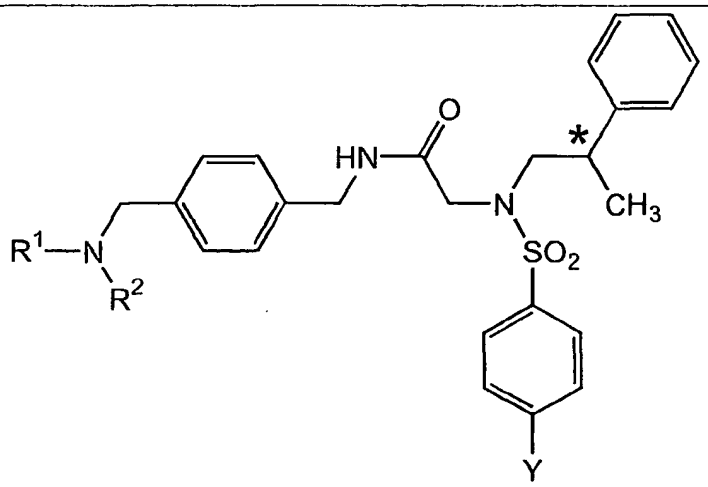
Cmpd #	Stereo	Y
366	R	2-methylphenyl
367	R	2-chlorophenyl
368	R	3-fluorophenyl
369	S	2-methylphenyl
370	S	2-chlorophenyl
371	S	3-fluorophenyl



Cmpd #	Y
320	2-methylphenyl
321	2-chlorophenyl
322	3-fluorophenyl

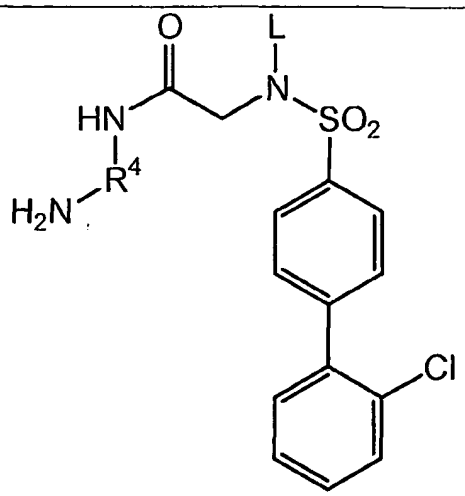


Cmpd #	Stereo	n	X
431	R	1	4-n-butyl
445	R	0	-
469	R	1	4-bromo
470	S	1	4-bromo
551	R	1	4-methoxy
552	R	1	4-trifluoromethyl
553	R	1	4-isopropyl
554	R	1	4-n-propyl
555	R	1	4-t-butyl
556	R	1	4-n-pentyl
557	R	1	3-methoxy
558	S	1	4-methoxy
559	S	1	4-trifluoromethyl
560	S	1	4-isopropyl
561	S	1	4-n-propyl
562	S	1	4-t-butyl
563	S	1	4-n-pentyl
564	S	1	3-methoxy



Cmpd #	R^1	R^2	Stereo	Y
471	methyl	methyl	R	2-chlorophenyl
472	ethyl	ethyl	R	2-chlorophenyl
473	H	methylcarbonyl	R	2-chlorophenyl

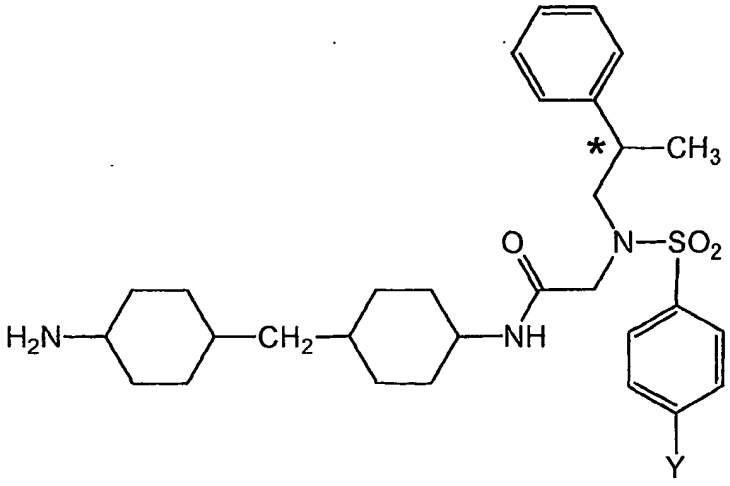
474	methyl	methyl	S	2-methylphenyl
475	ethyl	ethyl	S	2-methylphenyl
476	H	methylcarbonyl	S	2-methylphenyl



Cmpd #	R^4	L
483	-CH_2-(1,4-phenyl)-CH_2-	4-methyoxyphenylethyl
484	-CH_2-(1,4-phenyl)-CH_2-	3,6-dimethoxyphenylethyl
485	-CH_2-(1,4-phenyl)-CH_2-	2,3-dimethoxyphenylethyl
486	-CH_2-(1,4-phenyl)-CH_2-	1-cyclohexenylethyl
487	-CH_2-(1,4-phenyl)-CH_2-	3-bromo-4,5-dimethylphenylethyl
488	-CH_2-(1,4-phenyl)-CH_2-	2-chlorphenylethyl
489	-CH_2-(1,4-phenyl)-CH_2-	3-chlorophenylethyl
490	-CH_2-(1,4-phenyl)-CH_2-	2,4-dichlorophenylethyl
491	-CH_2-(1,4-phenyl)-CH_2-	2,6-dichlorophenylethyl
492	-CH_2-(1,4-phenyl)-CH_2-	2-trifluoromethylphenylethyl
493	-CH_2-(1,4-phenyl)-CH_2-	3,4-dimethylphenylethyl
494	-CH_2-(1,4-phenyl)-CH_2-	3,5-dimethylphenylethyl
495	-CH_2-(1,4-phenyl)-CH_2-	3-methoxyphenylethyl
496	-CH_2-(1,4-phenyl)-CH_2-	3-(2-chlorophenyl)-4,5-dimethoxyphenylethyl
501	n-hexyl	3,4-dimethoxyphenylethyl
502	n-hexyl	4-methoxyphenylethyl
503	n-hexyl	2,3-dimethoxyphenylethyl
504	n-hexyl	3-bromo-4,5-

		dimethoxyphenylethyl
505	n-hexyl	2-chlorophenylethyl
506	n-hexyl	3-chlorophenylethyl
507	n-hexyl	2,4-dichlorophenylethyl
508	n-hexyl	2,6-dichlorophenylethyl
509	n-hexyl	3,5-dimethoxyphenylethyl
510	n-hexyl	3-methoxyphenylethyl
511	n-hexyl	2,5-dimethoxyphenylethyl
512	n-hexyl	1-cyclohexenylethyl
513	n-hexyl	3-(2-chlorophenyl)-3,4-dimethoxyphenylethyl
514	n-hexyl	2-fluorophenylethyl
515	n-hexyl	2-trifluoromethylphenylethyl
527	$-CH_2$-(1,4-phenyl)-CH_2-	2-nitrophenylethyl
528	$-CH_2$-(1,4-phenyl)-CH_2-	2-aminophenylethyl
529	$-CH_2$-(1,4-phenyl)-CH_2-	2-dimethylaminophenylethyl
530	$-CH_2$-(1,4-phenyl)-CH_2-	2-(methylcarbonylamino) phenylethyl
531	$-CH_2$-(1,4-phenyl)-CH_2-	2-(methylsulfonylamino) phenylethyl
532	$-CH_2$-(1,4-phenyl)-CH_2-	CH_2-C$(CH_3)_2$-phenyl
533	$-CH_2$-(1,4-phenyl)-CH_2-	CH_2-C(OCH_3)-phenyl
534	$-CH_2$-(1,4-phenyl)-CH_2-	CH_2-CH(CH_3)-(2-methoxyphenyl)
535	$-CH_2$-(1,4-phenyl)-CH_2-	bicyclo[4.2.0]octa-1,3,5-triene
536	$-CH_2$-(1,4-phenyl)-CH_2-	CH_2-CH(cyclohexyl)-phenyl
537	$-CH_2$-(1,4-phenyl)-CH_2-	CH_2-CH(cyclobutyl)-phenyl
538	$-CH_2$-(1,4-phenyl)-CH_2-	CH_2-CH(ethyl)-phenyl
539	$-CH_2$-(1,4-phenyl)-CH_2-	2,3-dihydro-1H-indene
540	$-CH_2$-(1,4-phenyl)-CH_2-	CH$(phenyl)_2$
541	$-CH_2$-(1,4-phenyl)-CH_2-	2-methylphenylethyl
542	$-CH_2$-(1,4-phenyl)-CH_2-	3-fluorophenylethyl
543	$-CH_2$-(1,4-phenyl)-CH_2-	3,4-methylenedioxyphenyl
544	$-CH_2$-(1,4-phenyl)-CH_2-	2-pyridylethyl

545	-CH_2-(1,4-phenyl)-CH_2-	2-thienylethyl
546	-CH_2-(1,4-phenyl)-CH_2-	2-(N-methyl)-pyrrolidinylethyl
547	-CH_2-(1,4-phenyl)-CH_2-	phenylpropyl
548	-CH_2-(1,4-phenyl)-CH_2-	2-ethoxyphenylethyl
549	-CH_2-(1,4-phenyl)-CH_2-	3,4-dichlorophenylethyl
572	n-hexyl	CH_2-CH(OCH_3)-phenyl
573	n-hexyl	CH_2-CH(CH_3)-(2-methoxyphenyl)
574	n-hexyl	bicyclo[4.2.0]octa-1,3,5-triene
575	n-hexyl	CH_2-CH(cyclohexyl)-phenyl
576	n-hexyl	CH_2-CH(cyclobutyl)-phenyl
577	n-hexyl	CH_2-CH(ethyl)-phenyl
578	n-hexyl	2,3-dihydro-1H-indene
579	n-hexyl	CH_2-CH(phenyl)$_2$
580	n-hexyl	2-methylphenylethyl
581	n-hexyl	3-fluorophenylethyl
582	n-hexyl	3,4-methylenedioxyphenyl
583	n-hexyl	2-pyridylethyl
584	n-hexyl	2-thienylethyl
585	n-hexyl	2-(N-methylpyrrolidinyl)ethyl
586	n-hexyl	phenylpropyl
587	n-hexyl	2-ethoxyphenylethyl
588	n-hexyl	3,4-dichlorophenylethyl
589	n-hexyl	3-trifluoromethylphenylethyl

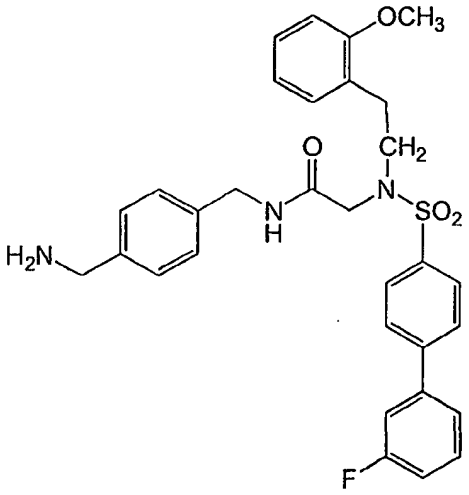


Cmpd #	Stereo	Y
497	R	2-chlorophenyl
498	R	2-methylphenyl
499	R	3-fluorophenyl
500	S	2-chlorophenyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

In a particularly preferred embodiment of the present invention are compounds of the formula (I) as enumerated in Table 2 below:

TABLE 2 (Structure and Compound #)



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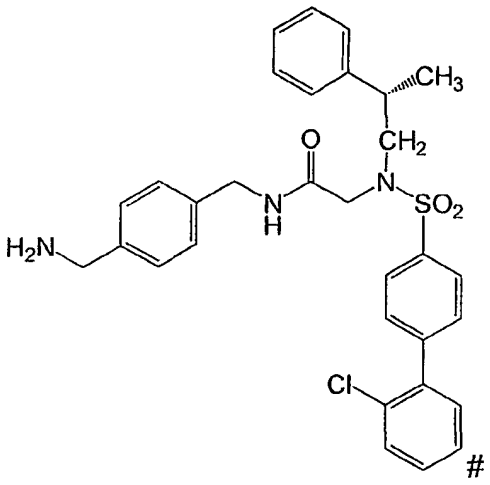

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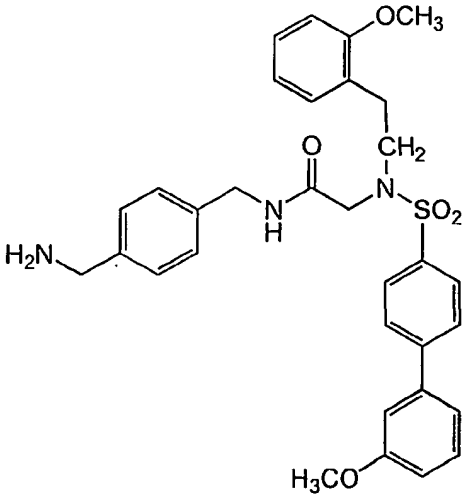

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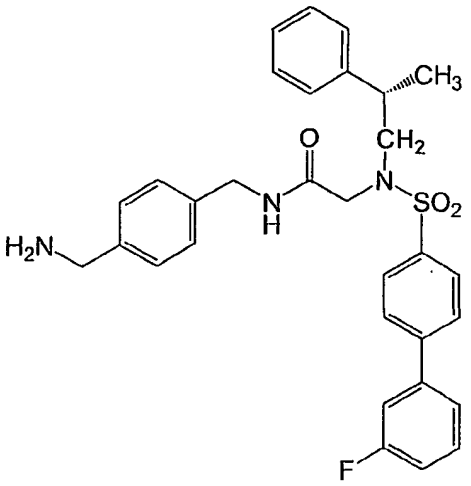

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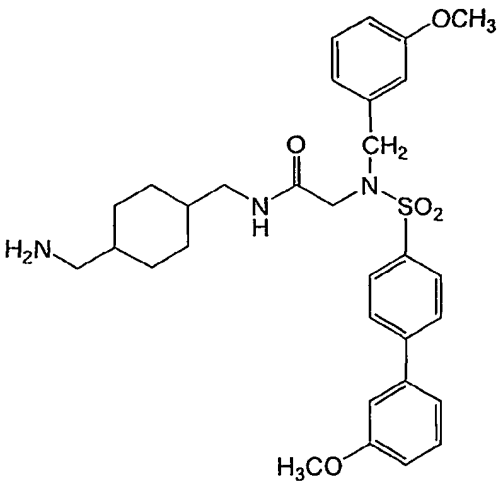

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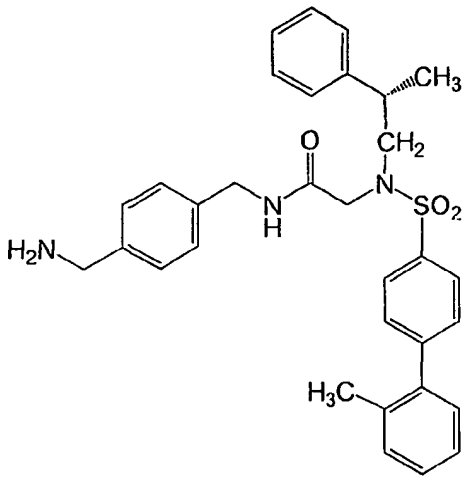

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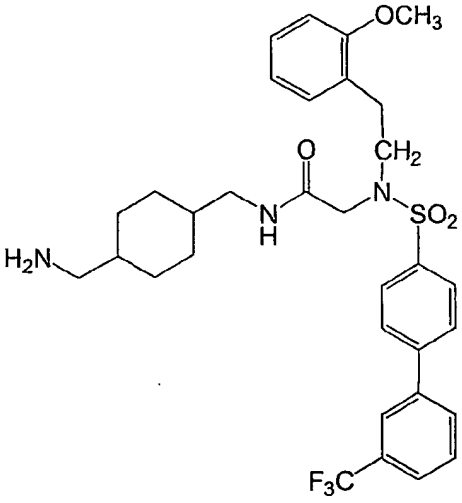

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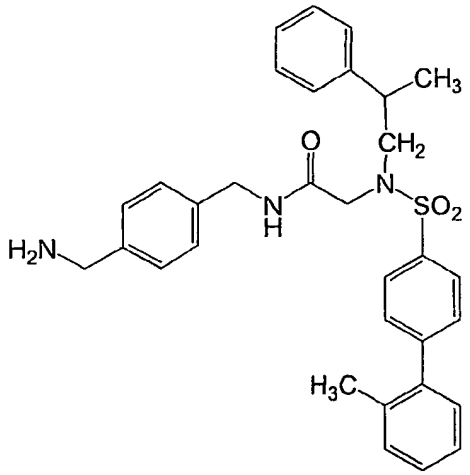

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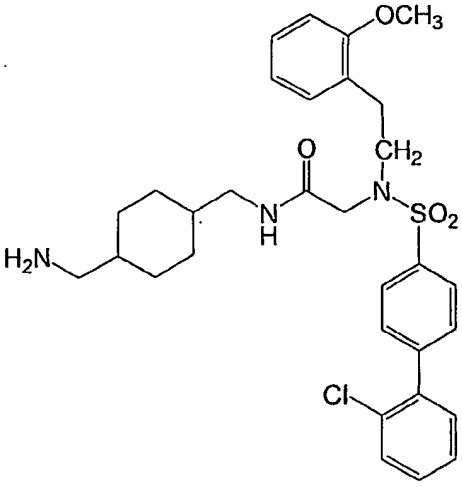

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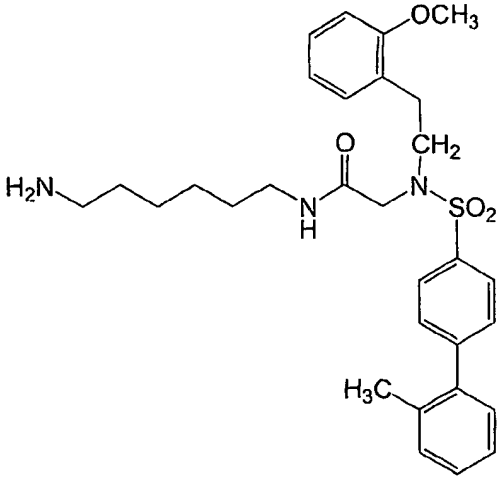

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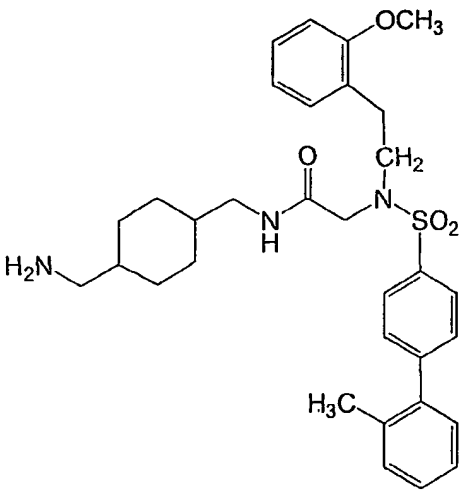

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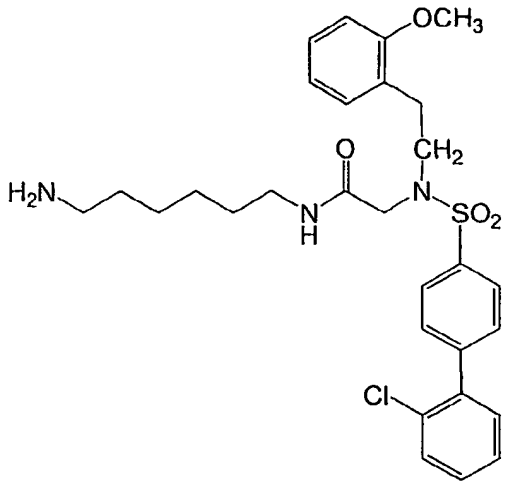

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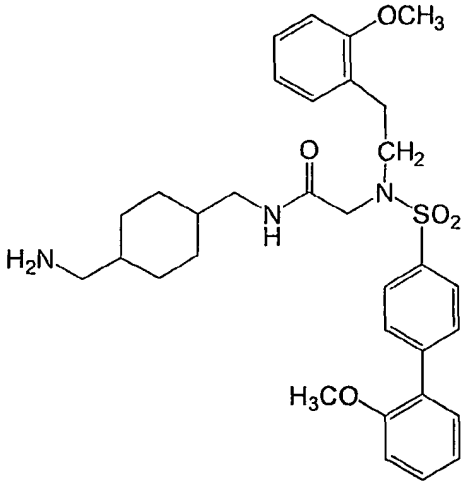

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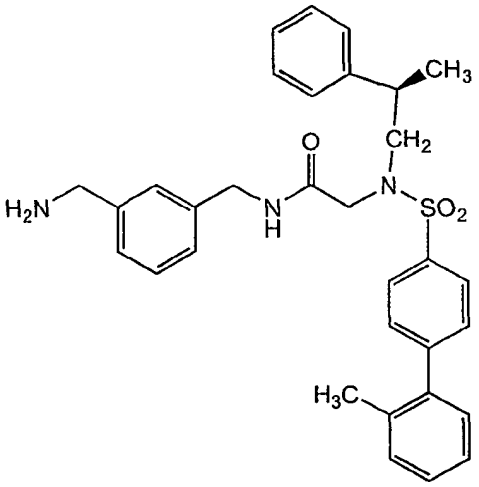

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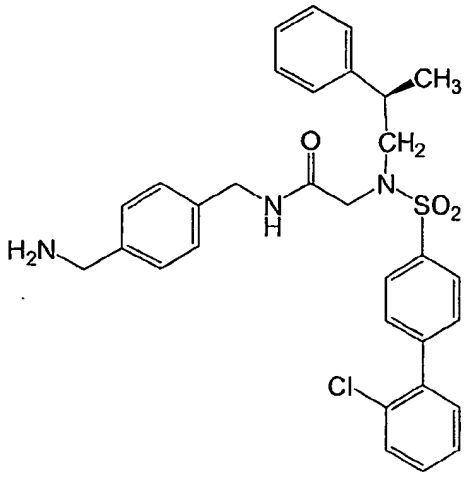
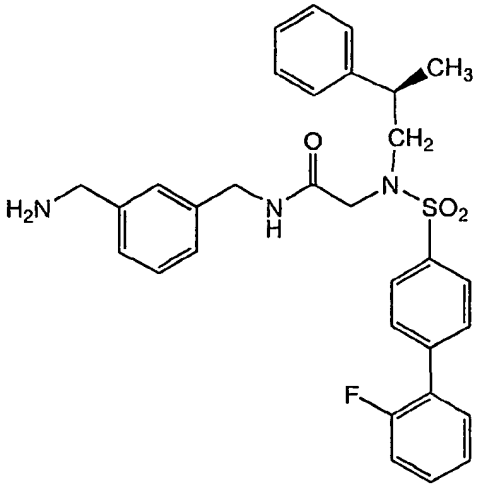


#198



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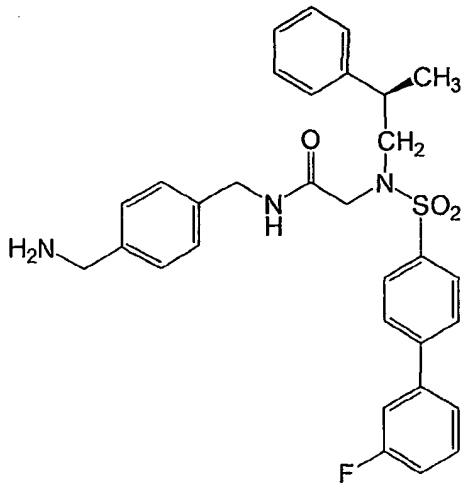

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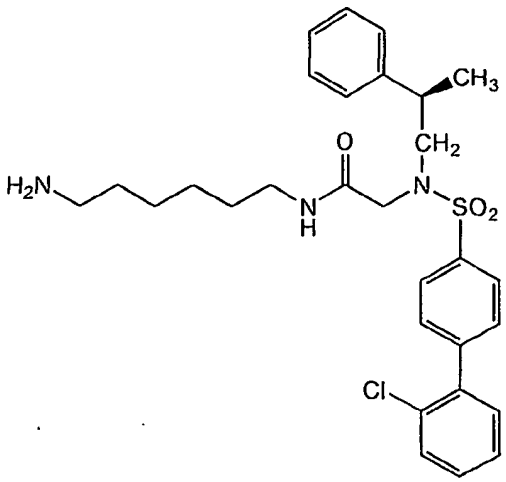


#397

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

For the compounds listed in Table 3 below, as well as all compounds listed in Table 1 and 2 above, structures were confirmed via molecular weight determination using an electro-spray mass spectrometer in positive mode and via HPLC retention time on a reversed phase column.

TABLE 3

Cmpd #	Meas MW MH^+	HPLC RT (min)	Cmpd #	Meas MW MH^+	HPLC RT (min)
39	460.47		297	618.3	
40	500.13, 502.10		298	618.2	
41	528.56, 530.27		299	618.2	
42	528.48, 530.28		300	564.1	
43	494.43, 496.16		301	546	
44	528.05, 530.16		302	564	
45	510.29		303	595.9, 597.9	
46	494.32, 496.16		304	596	
47	494.23, 496.16		305	570	
48	534.05, 536.12		306	546	
49	528.07, 530.11		307	564	
50	528.07, 530.12		308	595.9, 597.9	
51	528.07, 530.13		309	596	

	52	528.07, 530.14		310	570
	53	528.07, 530.15		311	542
	54	474.62, 476.30		312	561.9, 563.9
	55	474.62, 476.31		313	546
5	56	490.62, 492.37		314	576.0, 578.0
	57	510.57, 512.37		315	595.9, 597.9
	58	478.66, 480.23		316	579.9, 581.9
	59	520.45, 522.37		317	588.0, 590.0
	60	520.56, 522.33		318	608.0, 610.0
10	61	505.3		319	592.0, 594.0
	62	505.3		320	540
	63	505.3		321	559.9, 561.9
	64	586.45		322	544
	65	516.7		323	528
15	66	535.41		324	548.0, 549.9
	67	504.67, 506.39		325	532
	68	573.51		336	564.1
	69	478.68, 480.35		337	584.1, 586.1
	70	478.68, 480.36		338	580.1
20	71		3.325	339	618.1, 620.1
	72		3.348	340	550.1
	73		3.315	341	570.0, 572.0
	74	52.45, 524.28		342	566.1
	75	514.34, 516.29		343	604.1, 606.1
25	76	538.47, 540.32		344	558.1
	77	526.58, 528.32		345	578.0, 580.0
	78	568.03		346	574.1
	79	538.42, 540.36		347	612.1, 614.1
	80	522.57, 524.34		348	544.1
30	81	558.56, 560.31		349	564.0, 566.0
	82	542.26, 544.13		350	560.1
	83	509.14		351	598.0, 600.0
	84	514.16		352	538.2, 538.2

	85	565.5, 567.30		353	558.1, 560.1
					558.1, 560.1
	86	508.47, 510.29		354	554.1
	87	542.19, 544.07		355	592.0, 594.0
5	88	527.44, 530.22		356	524.2
	89		3.206	357	544.1, 546.1
	90	533.40, 535.30		358	540.1
	91	509.14		359	578.0, 580.0
	92	538.46, 540.34		366	574.2
10	93	523.16		367	594.1, 596.1
	94	536.54		368	578.1
	95	528.31, 530.28		369	574.1
	96	552.48, 55434		370	594.1, 596.1
	97	540.44, 542.34		371	578.1
15	98	582.07		372	548.2
	99	552.67, 554.32		373	568.1, 570.1
					568.1, 570.1
	100	536.53, 538.37		374	552.1
	101	572.43, 574. 23		375	548.2
20	102	556.25, 558.04		376	568.1, 570.0
	103	523.16		377	552.1
	104	528.3		378	508.2
	105		3.158	379	526.1
	106	522.42		380	512.1
25	107	556.20, 558.01		381	508.2
	108	541.34, 543.37		382	528.1, 530.1
	109		3.293	383	512.1
	110	547.22		384	548.2
	111	523.2		385	568.1, 570.0
30	112	552.37		386	552.1
	113	537.18		387	548.1
	114	508.0, 510.0		388	568
	115	536.1		389	552.1

	116	536.1		390	542.1, 542.1
	117	502.1, 504.1		391	564
	118	536.0, 538.0		392	546, 546.0
	119	518.1		393	542.1
5	120	502.1, 504.1		394	562.0, 564.0
	121	528.1		395	546
	122	536.0, 538.0		396	522.2, 522.2
	123	536.0, 538.1		397	542.1, 544.1
					542.1, 544.1
10	124	536.0, 538.2		398	526.1, 526.1
	125	536.0, 538.3		399	522.2
	126	541.9, 543.9		400	542.1, 544.1
	127	482.2		401	526.1
	128	498.2		402	528.1, 530.2.
15	129	518.1		412	528.2
	130	486.2		413	573.1
	131	486.2		414	546.1
	132	486.2		415	542.2
	133	528.1		416	596.1
20	134	513.1		417	596.1
	135	513.1		418	562.1
	136	513.1		419	558.1
	137	594		420	596.1
	138	524.2		421	558.1
25	139	543.1		422	612.1
	140	512.2		423	546.1
	141		2.946	424	578.1
	142	581		425	580
	143	536.1		426	606
30	144	552		427	562
	145	551		428	596
	146	598.1		429	596
	147	474.1		430	664

	148	482.2	431	508.1
	149	502.1, 504.1	432	568.1
	150	468.1	433	663
	151	508.2	434	553.1
5	152	500.1	435	553.1
	153	524.1	436	572
	154	512.1	437	655.1
	155	554.1	438	547.1
	156	524.1	439	586
10	157	508.2	440	529.1
	158	544.1	441	618.1
	159	528.1, 530.1	442	650
	160	495.2	443	532
	161	500.1	444	548.1
15	162	551.1	445	452.1
	163	494.2	446	634.1
	164	528.1	447	666
	165	513.1	448	634.1
	166	528.1, 530.0	449	584
20	167	519.1	450	588.1
	168	495.2	451	546.1
	169	524.1	452	578.1
	170	509.1	453	558.1
	171	512.1	454	580
25	172	512.1	455	573
	173	538.1	456	604.1
	174	494.2	457	657.1
	175	486.1	458	657.1
	176	510.1	459	546.1
30	177	498.1	460	588.1
	178	540.1	461	685.2
	179	510.1	462	574
	180	494.2	463	570.1

	181	530.1	464	542.2
	182	514.1, 516.2	465	542.1
	183	481.1	466	539.2
	184	486.1	467	543.2
5	185	537.1	468	585.1
	186	480.2	469	530.31, 532.31
	187	514.1, 516.0	470	530.31, 532.32
	188	499.1	471	590.54, 592.54
	189	514.1, 516.0	472	618.59, 620.57
10	190	505.1	473	604.52, 606.54
	191	481.1	474	570.59
	192	510.1	475	598.64
	193	495.2	476	584.57
	194	498.1	477	526.5, 528.5
15	195	498.1	478	506.6
	196	524.1	479	510.6
	197	528.2	480	606.5, 608.5
	198	562.1, 564.0 562.4,564.4	481	614.5, 616.5
20	199	562.1, 564.1	483	578.5, 580.4
	200	558.1	484	608.5, 610.5
	201	558.1	485	608.5, 610.5
	202	558.1	486	552.5, 554.5
	203	546.1	487	686.5, 688.5
25	204	546.1	488	582.4, 584.4
	205	542.1	489	582.4, 584.4
	206	542.1	490	616.5, 618.5
	207	528.1	491	616.5, 618.4
	208	562.1, 564.0	492	616.5, 618.5
30	209	562.1, 564.1	493	622.6, 624.6
	210	558.1	494	608.5, 610.5
	211	558.1	495	578.4, 580.4
	212	558.1	496	718.6, 720.6

	213	546.1		497	636.7
	214	546.1		498	616.7
	215	542.1, 542.5		499	620.9
	216	542.1		500	636.7
5	217		3.418	501	602.6, 604.5
	218		3.509	502	558.5, 560.5
	219		3.403	503	588.5, 590.5
	220		3.413	504	666.6, 668.6
	221		3.450	505	562.4, 564.4
10	222		3.465	506	562.4, 564.4
	223		3.539	507	596.4, 598.4
	224		3.575	508	596.5, 598.5
	225	578.1, 580.1		509	588.5, 590.5
	226	574.1		510	558.5, 560.5
15	227	559.1		511	588.5, 560.5
	228	562.1		512	532.5, 534.5
	229	562.1		513	698.7, 700.7
	230	588.1		514	546.5. 548.5
	231	578.1, 580.1		515	596.5, 598.5
20	232	544.1		521	576.5, 578.5
	233	563.1		522	576.5, 578.5
	234	569.1		523	576.5, 578.6
	235	545.1		524	576.5, 578.7
	236	634.3		525	576.5, 578.8
25	237	569.1		526	576.5, 578.9
	238	604.2		527	592.9, 594.9
	239	612.1, 614.1		528	563.0, 565.5
	240	612.2		529	590.9, 592.9
	241	612.2		530	604.9, 606.9
30	242	612.2		531	640.9, 642.9
	243	558.1		532	576.0, 577.9
	244	558.2		533	578, 0, 580.0
	245	550.1		534	592.0, 594.0

	246	574.2	535	560.0, 562.0
	247	562.1	536	616.0, 618.0
	248	574.2	537	587.9, 589.9
	249	558.2	538	576.0, 578.0
5	250	594.2	539	560.0, 562.0
	251	578.1, 580.1	540	623.9, 625.9
	252	545.2	541	562.0, 564.0
	253	578.1, 580.1	542	566.0, 567.9
	254	574.2	543	591.9, 593.9
10	255	559.2	544	549.0, 551.0
	256	562.1	545	554.0, 555.9
	257	562.1	546	555.0, 557.0
	258	588.2	547	562.0, 564.0
	259	578.1	548	591.9, 593.9
15	260	544.2	549	615.8, 617.8
	261	563.2	550	582.6
	262	569.2	551	482.6
	263	545.2	552	520.5
	264	534.4	553	494.6
20	265	569.1	554	494.6
	266	604.3, 605.3	555	508.6
	267	612.3	556	522.6
	268	612.3	557	482.6
	269	612.3	558	482.6
25	270	558.2	559	520.5
	271	554.0, 556.1	560	494.5
	272	564.1	561	494.6
	273	556.1	562	508.6
	274	580.2	563	522.6
30	275	568.1	564	482.5
	276	580.2	572	558.4, 560.0
	277	564.1	573	572.0, 574.0
	278	600.2	574	540.5, 542.1

	279	584.1, 586.1		575	596.4, 598.0
	280	551.1		576	569.2, 571.0
	281	584.1, 586.1		577	557.0, 559.1
	282	580.2		578	540.5, 542.1
5	283	565.1		579	604.3
	284	568.1		580	542.4, 544.1
	285	568.1		581	547.1, 549.0
	286	594.2		582	572.0, 574.0
	287	584.1, 586.1		583	529.0, 531.0
10	288	550.1		584	534.0, 536.0
	289	569.1		585	535.1, 537.1
	290	575.1		586	542.5, 544.1
	291	551.1		587	572.0, 574.0
	292	640.4		588	596.0, 597.9
15	293	575.1		589	596.3, 597.9
	294		3.315	590	507.6
	295	610.2		591	507.6
	296		4.021		

20 The salts of the compounds of this invention refer to non-toxic "pharmaceutically acceptable salts." Other salts may, however, be useful in the preparation of compounds according to this invention or of their pharmaceutically acceptable salts. Suitable pharmaceutically acceptable salts of the compounds include acid addition salts which may, for example, be
25 formed by mixing a solution of the compound with a solution of a pharmaceutically acceptable acid such as hydrochloric acid, sulfuric acid, fumaric acid, maleic acid, succinic acid, acetic acid, benzoic acid, citric acid, tartaric acid, carbonic acid or phosphoric acid. Furthermore, where the compounds of the invention carry an acidic moiety, suitable pharmaceutically
30 acceptable salts thereof may include alkali metal salts, e.g., sodium or potassium salts; alkaline earth metal salts, e.g., calcium or magnesium salts; and salts formed with suitable organic ligands, e.g., quaternary ammonium

salts. Thus, representative pharmaceutically acceptable salts include the following:

acetate, benzenesulfonate, benzoate, bicarbonate, bisulfate, bitartrate, borate, bromide, calcium edetate, camsylate, carbonate, chloride, clavulanate, citrate, dihydrochloride, edetate, edisylate, estolate, esylate, fumarate, gluceptate, gluconate, glutamate, glycollylarsanilate, hexylresorcinate, hydrabamine, hydrobromide, hydrochloride, hydroxynaphthoate, iodide, isothionate, lactate, lactobionate, laurate, malate, maleate, mandelate, mesylate, methylbromide, methylnitrate, methylsulfate, mucate, napsylate, nitrate, N-methylglucamine ammonium salt, oleate, pamoate (embonate), palmitate, pantothenate, phosphate/diphosphate, polygalacturonate, salicylate, stearate, sulfate, subacetate, succinate, tannate, tartrate, teoclate, tosylate, triethiodide and valerate.

The pharmaceutically acceptable esters of the novel compounds of the present invention include such as would be readily apparent to a medicinal chemist, and include, for example, those described in detail in US Pat. No. 4,309,43, Column 9, line 61 ot Column 12, line 51, which is incorporated herein by reference. Included within such pharmaceutically acceptable esters are those hydrolyzed under physiological conditions, such as pivaloyloxymethyl, acetoxymethyl, phthalidyl, indanyl and methoxymethyl, and those described l detail in U.S. Patent No. 4.479.947, which is incorporated herein by reference.

The present invention includes within its scope prodrugs of the compounds of this invention. In general, such prodrugs will be functional derivatives of the compounds which are readily convertible *in vivo* into the required compound. Thus, in the methods of treatment of the present invention, the term "administering" shall encompass the treatment of the various disorders described with the compound specifically disclosed or with a compound which may not be specifically disclosed, but which converts to the specified compound *in vivo* after administration to the patient. Conventional procedures for the selection and preparation of suitable prodrug derivatives are described, for example, in "Design of Prodrugs", ed. H. Bundgaard, Elsevier, 1985.

Where the compounds according to this invention have at least one chiral center, they may accordingly exist as enantiomers. Where the compounds possess two or more chiral centers, they may additionally exist as diastereomers. It is to be understood that all such isomers and mixtures thereof are encompassed within the scope of the present invention. Furthermore, some of the crystalline forms for the compounds may exist as polymorphs and as such are intended to be included in the present invention. In addition, some of the compounds may form solvates with water (i.e., hydrates) or common organic solvents, and such solvates are also intended to be encompassed within the scope of this invention.

Where the processes for the preparation of the compounds according to the invention give rise to mixture of stereoisomers, these isomers may be separated by conventional techniques such as preparative chromatography. The compounds may be prepared in racemic form, or individual enantiomers may be prepared either by enantiospecific synthesis or by resolution. The compounds may, for example, be resolved into their component enantiomers by standard techniques, such as the formation of diastereomeric pairs by salt formation with an optically active acid, such as (-)-di-p-toluoyl-d-tartaric acid and/or (+)-di-p-toluoyl-l-tartaric acid followed by fractional crystallization and regeneration of the free base. The compounds may also be resolved by formation of diastereomeric esters or amides, followed by chromatographic separation and removal of the chiral auxiliary. Alternatively, the compounds may be resolved using a chiral HPLC column.

It is intended that the definition of any substituent or variable at a particular location in a molecule be independent of its definitions elsewhere in that molecule. It is understood that substituents and substitution patterns on the compounds of this invention can be selected by one of ordinary skill in the art to provide compounds that are chemically stable and that can be readily synthesized by techniques known in the art as well as those methods set forth herein.

Abbreviations used in the specification, particularly the Schemes and Examples, are as follows:

TABLE 4

Abbreviation		Definition
BOC	=	Butoxycarbonyl
Cmpd #	=	Compound Number
DCE	=	Dichloroethane
DCM	=	Dichloromethane
DIEA	=	Diisopropylethylamine
DMAC	=	Dimethylacetamide
DMAP	=	4-Dimethylaminopyridine
DMF	=	Dimethylformamide
DMSO	=	Dimethylsulfoxide
EDTA	=	Ethylenediamine-N,N,N",N"-tetraacetic acid
Fmoc	=	9-Fluorenyl methoxycarbonyl
h-FSHR	=	human Follicle Stimulating Hormone Receptor
FMPB	=	4-(4-Formyl-3-methoxyphenyoxy)butyryl
HATU	=	2-(1H-Benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate
HPLC RT	=	High Pressure Liquid Chromatography Retention Time
Mol. Wt.	=	Measured Molecular Weight
PBF	=	2,2,4,6,7-Pentamethyldihydrobenzofuran-5-sulfonyl
Stereo	=	Optical Configuration of Stereogenic Center
TMOF	=	Trimethylorthoformate

The substituted aminoalkylamide derivatives of this invention are capable of inhibiting follicle stimulating hormone (FSH) to achieve the desired pharmacological effect. With an effective amount of the substituted aminoalkylamide derivative compounds dispersed in a pharmaceutical composition as an active ingredient, the pharmaceutical composition is introduced as a unit dose into an afflicted mammal.

The term "unit dosage" and its grammatical equivalent is used herein to refer to physically discrete units suitable as unitary dosages for human patients and other warm blooded mammals, each unit containing a predetermined effective, pharmacologic amount of the active ingredient calculated to produce

the desired pharmacological effect in association with the required physiologically tolerable carrier, e.g., a diluent or a vehicle. The specifications for the novel unit dosage forms suitable for use herein are dictated by and are directly dependent on (a) the unique characteristics of the active ingredient, and (b) the limitations inherent in the art of compounding such an active ingredient for therapeutic use in humans and other mammals. Examples of suitable unit dosage form in accord with this invention are tablets, capsules, pills, powder packets, granules, wafers, sterile parenteral solutions or suspensions, metered aerosol or liquid sprays, drops, ampoules, autoinjector devices or suppositories; for oral parenteral, intranasal, sublingual or rectal administration, or for administration by inhalation or insufflation and the like. The active ingredient is referred to herein as being dispersed in the carrier. The dispersion form can be a simple admixture, a non-settling dispersion as in the case of certain emulsions, or as an ultimate dispersion, a true solution.

The amount of active ingredient that is administered in vivo depends on the age and weight of the mammal treated, the particular medical condition to be treated, the frequency of administration, and the route of administration. The dose range can be about 0.01 to about 500 milligrams per kilogram of body weight, more preferably about 0.1 to about 50 milligrams per kilogram of body weight and most preferably about 0.1 to about 25 milligrams per kilogram of body weight. The human adult dose is in the range of about 10 to about 2000 milligrams daily, given as a single dose or in 3 or 4 divided doses. Veterinary dosages correspond to human dosages with the amounts administered being in proportion to the weight of the animal as compared to adult humans. When the compounds are employed to treat FSH receptor mediated diseases or disorders the dosage range can be about 0.01 to about 200 mg/kg. The preferred dosage range is from about 0.5 to about 100 mg/kg.

Physiologically tolerable carriers are well known in the art. Carriers may be divided into liquid and solid carriers.

Exemplary of liquid carriers are aqueous solutions that contain no materials in addition to the substituted aminoalkylamide derivative compound, or contain a buffer such as sodium phosphate ay a physiological pH value, saline and the like. Liquid compositions can also contain liquid phases in

addition to and to the exclusion of water. Exemplary of such additional liquid phases are glycerin and vegetable oils such as cottonseed oil.

Exemplary solid carriers (diluents) include those materials usually used in the manufacture of pills or tablets, and include corn starch, lactose, dicalcium phosphate, thickeners, such as tragacanth and methylcellulose U.S.P., finely divided SiO_2, polyvinylpyrrolidone, magnesium stearate and the like. Antioxidants such as methylparaben and propylparaben can be present in both solid and liquid compositions, as can sweeteners such as cane or beet sugar, sodium saccharin, sodium cyclamate and the dipeptide methyl ester sweetener sold under the trademark NUTRASWEET (aspartame) by G. D. Searle Co.

The pharmaceutical composition can be administered orally, topically or by injection, by means well known in the art. In preferred practice, the composition is administered orally as a tablet, capsule or aqueous dispersion. The pharmaceutical composition is maintained within the mammal until the substituted aminoalkylamide derivative compound is cleared from the mammal's body by natural means such as excretion or metabolism.

Compositions for injection may be prepared in unit dosage form in ampules or in multidose containers. The compositions may take such forms as suspensions, solutions, or emulsions in oily or aqueous vehicles, and may contain formulatory agents. Alternatively, the active ingredient may be in a powder form for reconstitution, at the time of delivery, with a suitable vehicle, such as sterile water. Topical formulations may be formulated in hydrophobic or hydrophilic bases as ointments, creams, lotions, paints, or powders.

The compounds of the present invention can also be administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamellar vesicles, and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids, such as cholesterol, stearylamine or phophatidylcholines.

Compounds of the present invention may also be delivered by the use of monoclonal antibodies as individual carriers to which the compound molecules are coupled. The compounds of the present invention may also be coupled with soluble polymers as targetable drug carriers. Such polymers can include polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamidephenol,

polyhydroxyethylaspartamidephenol, or polyethyl-eneoxidepolylysine substituted with palmitoyl residue. Furthermore, the compounds of the present invention may be coupled to a class of biodegradable polymers useful in achieving controlled release of a drug, for example, polylactic acid, polyepsilon caprolactone, polyhydroxy butyric acid, polyorthoesters, polyacetals, polydihydropyrans, polycyanoacrylates and cross-linked or amphipathic block copolymers of hydrogels.

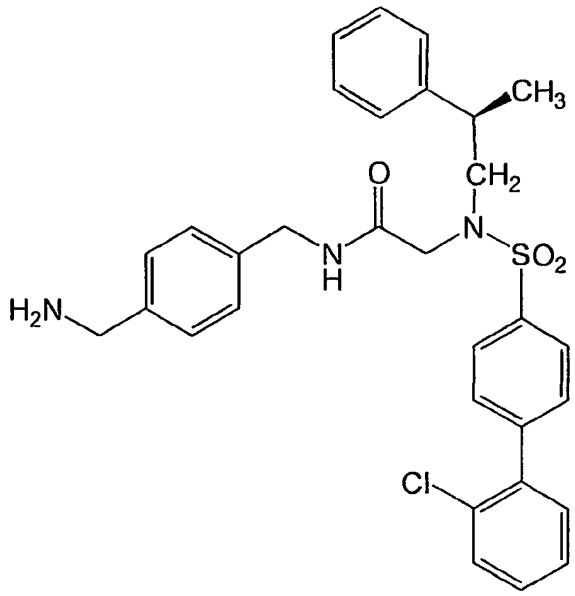
Inasmuch as a pharmaceutical composition can be administered 3 to 4 times daily (per 24 hour period), the method of treating a disorder of condition mediated by FSH can include administering the pharmaceutical composition a plurality of times into the treated mammal over a time period of weeks, months and years.

Disorders or conditions mediated by the FSH receptor include uterine fibroids, endometriosis, polycystic ovarian disease, dysfunctional uterine bleeding, breast cancer and ovarian cancer; depletion of oocytes (a common side effect of chemotherapy or similar treatment); spermatocyte depletion; or for female and male contraception.

The following examples are set forth to aid in the understanding of the invention, and are not intended and should not be construed to limit in any way the invention set forth in the claims which follow thereafter.

EXAMPLE 1

COMPOUND #198



A. Preparation of Amino Carbamate resin

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,4-xylenediamine (5.44 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid , 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Optically Pure Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added (R)-β-methylphenethylamine (5.408 g, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3

portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3 portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Bromophenylsulfonamide Resin

The optically pure resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) and then 4-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole). The suspension was shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Sulfonamide Resin

The N-(R)-β-methylphenthyl-4-bromophenyl-sulfonamide resin (from D) was split into 10 portions, each containing 0.133 millimole of resin. To one portion was added 2-chlorobenzeneboronic acid (0.076 g, 0.399 millimole). To the solution was then added palladium tetrakistriphenylphosphine (0.0154, 0.0133 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (0.830 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 301-310 were prepared according to the above procedure with appropriate selection and substitution of suitably substituted benzeneboronic acid in Step E.

Compounds 311-319 were similarly prepared according to the procedure above with appropriate selection and substitution of a racemic mixture of suitably substituted phenethylamine in Step C and appropriate selection and substitution of suitably substituted benzeneboronic acid in Step E.

Compounds 412 through 468 may similarly be prepared according to the procedure described above, with appropriate selected and substitution of a suitably substituted boronic acid in Step E.

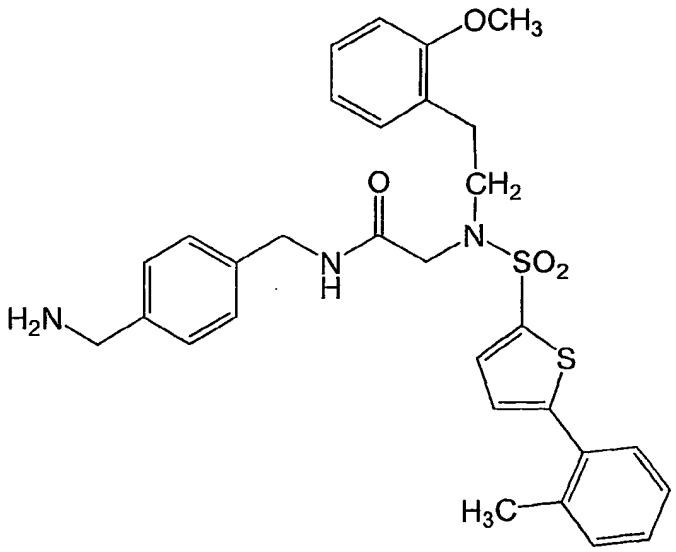
Compounds 469-470 were similarly prepared according to the procedure above, with appropriate selection and substitution of reagents. Compound 469 was prepared from the product of Step D, Compound 470 was prepared by substituting (S)-β-methylphenethylamine for (R)-β-methylphenethylamine in Step C.

Compounds 483-496 were similarly prepared according to the procedure above, with appropriate selection and substitution of suitably substituted phenethylamines in step C. Compounds 527-549 were similarly prepared according to the procedure above with appropriate selection and substitution of suitably substituted phenethylamines in step C.

Compounds 522-526 were similarly prepared according to the procedure above, with appropriate selection and substitution of reagents.

EXAMPLE 2

COMPOUND #272



A. Preparation of Amino Carbamate Resin.

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,4-xylenediamine (5.44 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for

24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic acid.

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added 2-(2-methoxy)phenethylamine (5.408 g, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3 portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of Sulfonamide Resin

The resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) followed by 5-bromo-2-thiophenesulfonyl chloride (5.23 g, 20.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Substituted Phenylsulfonamide Resin

The 4-bromophenylsulfonamide resin (from D) was split into 23 portions, each containing 0.174 millimole of resin. To one portion was added 2-methylbenzeneboronic acid (0.089 g, 0.522 millimole). To the solution was then added palladium tetrakistriphenylphosphine (0.020 g, 0.0174 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (1.086 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

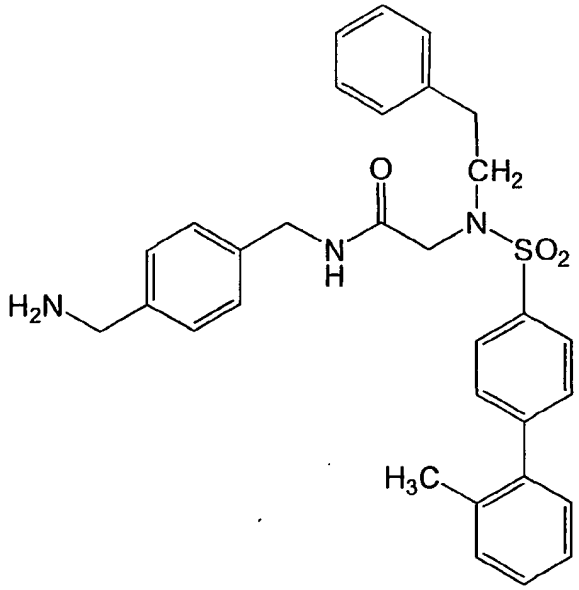
F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 271, 273-300 were prepared according to the process above with appropriate selection and substitution of a suitably substituted boronic acid in Step E.

EXAMPLE 3

COMPOUND #205



A. Preparation of Amino Carbamate Resin.

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,4-xylenediamine (5.44 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid , 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic acid.

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the secondary amine

The 2-bromoacetylated resin (from B) was swelled in DMSO (approximately 150 ml). To the suspension was added phenethylamine (6.045 g, 40 millimoles) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions methanol, 3 portions DCM/5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

D. Preparation of bromophenylsulfonamide Resin

The resin-bound secondary amine (from C) was swelled in DCM (approximately 200 ml). To the suspension was added pyridine (3.19 g) followed by 4-bromophenylsulfonylchloride (5.1 g, 20 millimoles) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Sulfonamide Resin

The resin-bound secondary amine (from D) was split into 10 portions, each containing 0.133 millimole of resin. To one portion was 2-methylbenzeneboronic acid (0.056 g, 0.399 millimoles). To the solution was then added palladium tetrakistriphenylphosphine (0.0154, 0.0133 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (0.830 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1

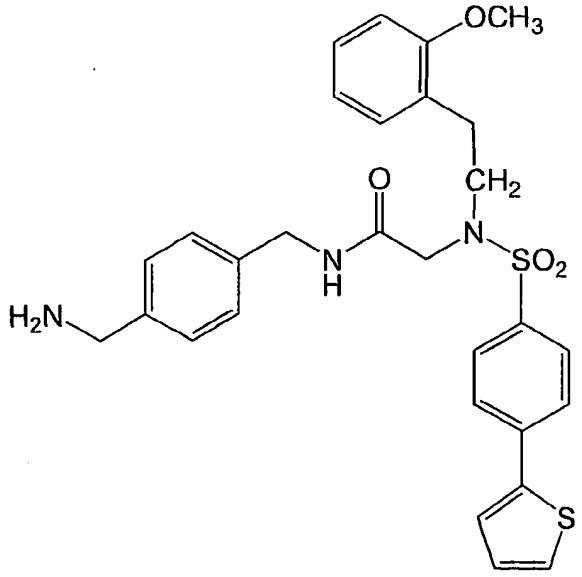
water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 197, 199-204, 206-216 and 323-325 were prepared according to the above procedure, with appropriate selection and substitution of a suitably substituted benzeneboronic acid in Step E

Compounds 412 through 468 may alternatively be prepared according to the procedure described in Example 3 above, with substitution of (R)-β-methylphenylethylamine in Step C and appropriate selected and substitution of a suitably substituted boronic acid in Step E.

EXAMPLE 4

COMPOUND #245



A. Preparation of Amino Carbamate Resin.

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,4-xylenediamine (5.44 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid , 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic acid.

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the secondary amine

(Displacement of bromide by 2-(2-methoxy)phenethylamine)

The 2-bromoacetylated resin (from B) was swelled in DMSO (approximately 150 ml). To the suspension was added 2-(2-methoxy)phenethylamine (6.045 g, 40 millimoles) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions methanol, 3 portions DCM/5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

D. Preparation of bromophenylsulfonamide Resin

The resin-bound secondary amine (from C) was swelled in DCM (approximately 200 ml). To the suspension was added pyridine (3.19 g) followed by 3-bromophenylsulfonylchloride (5.1 g, 20 millimoles) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Sulfonamide Resin

The 3-bromophenylsolfonamide resin (from D) was split into 30 portions, each containing 0.133 millimoles of resin. To one portion was added 2-thiopheneboronic acid (0.051 g, 0.399 millimoles). To the solution was then added palladium tetrakistriphenylphosphine (0.0154 g, 0.133 millimoles), DME (2.5 ml) and 2M sodium carbonate solution in water (0.830 ml). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

F. Cleavage of the Resin Support

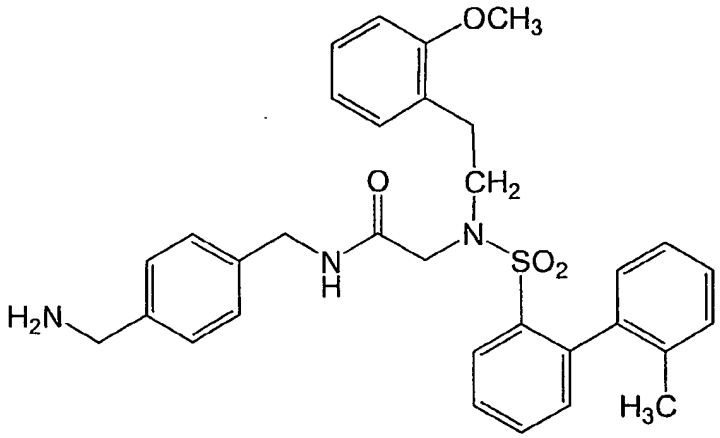
The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80

YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 10-19, 145-146, 217, 219-244 and 246-270 were prepared according to the above procedure with appropriate selection and substitution of bromophenylsulfonyl chloride in step D and by appropriate selection and substitution of a suitably substituted boronic acid in step E.

EXAMPLE 5

COMPOUND #218



A. Preparation of Amino Carbamate Resin

Wang p-nitrophenylcarbonate resin (4.0 millimole) was swelled in DMF (200 mL). To the suspension was added 1,4-xylenediamine (5.45 g, 40.0 millimole) dissolved in DMF (75 mL). The mixture was shaken for 24 hours. The solvent was removed by filtration. The resin was washed with 3 portions of DMF, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3 portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added 2-methoxyphenethylamine (6.05 g, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3 portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 2-Bromophenylsulfonamide Resin

The resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) followed by 2-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Substituted Phenylsulfonamide Resin

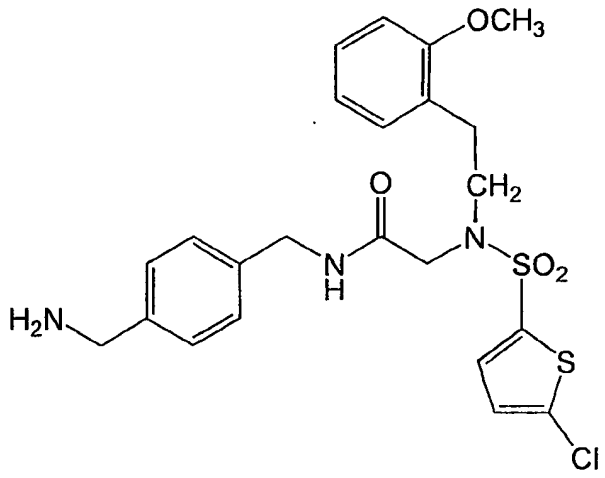
The 2-bromophenylsulfonamide resin (from D) was split into 23 portions, each containing 0.174 millimole of resin. To one portion was added 2-methylbenzneboronic acid (0.071 g, 0.522 millimole). To the solution was then added palladium tetrakistriphenylphosphine (0.020, 0.0174 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (1.086 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

EXAMPLE 6

COMPOUND #114



A. Preparation of Amino Carbamate Resin.

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,4-xylenediamine (5.44 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid , 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic acid.

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the secondary amine

(Displacement of bromide by 2-(2-methoxy)phenethylamine)

The 2-bromoacetylated resin (from B) was swelled in DMSO (approximately 150 ml). To the suspension was added 2-(2-methoxy)phenethylamine (6.045 g, 40 millimoles) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions methanol, 3 portions DCM/5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

D. Preparation of Sulfonamide Resin

The resin bound secondary amine (from C) was split into 36 portions each containing 0.111 millimole of resin. One portion was swelled in DCM (1.5 ml). To the suspension was added pyridine (0.089 g), followed by 5-chlorothiophene-2-sulfonyl chloride (0.121 g, 0.556 millimoles) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Cleavage of the Resin Support

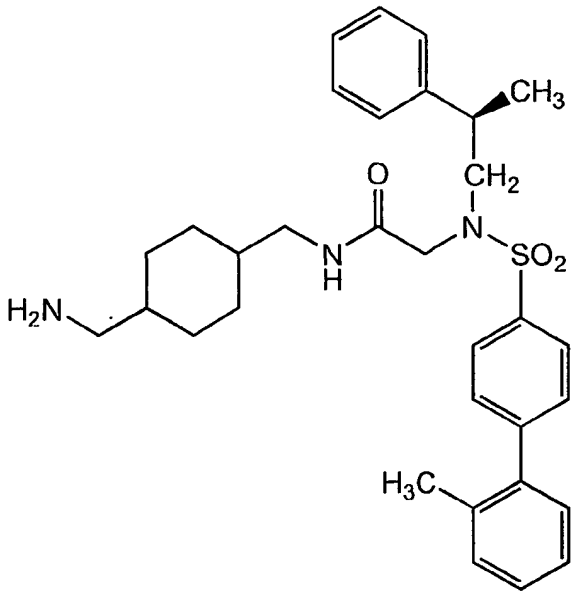
The product was cleaved from the resin using a cleaving cocktail solution of 90:10 TFA:water. The cleavage solution was evaporated. The product was purified by semi-preparative reversed phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product wa lyophilized and analyzed by ES/MS and reversed phase HPLC.

Compounds 115-144 and 147-150 were prepared according the above procedure with appropriate selection and substitution of a suitably substituted sulfonyl chloride in Step D.

Compounds 550-564 were similarly prepared according to the procedure above with appropriate selection and substitution of suitably substituted phenethylamines in step C and appropriate selection and substitution of suitably substituted sulfonyl chlorides in step D.

EXAMPLE 7

COMPOUND #372



A. Preparation of Amino Carbamate resin

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,4-cyclohexylmethylamine (5.69 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Optically Pure Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added (R)-β-methylphenethylamine (5.408 g, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3

portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Bromophenylsulfonamide Resin

The optically pure resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) and then 4-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole). The suspension was shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Substituted Phenylsulfonamide Resin

The N-(R)-β-methylphenthyl-4-bromophenyl-sulfonamide resin (from D) was split into 10 portions, each containing 0.133 millimole of resin. To one portion was 2-methylbenzeneboronic acid (0.076 g, 0.399 millimole). To the solution was then added palladium tetrakistriphenylphosphine (0.0154, 0.0133 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (0.830 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

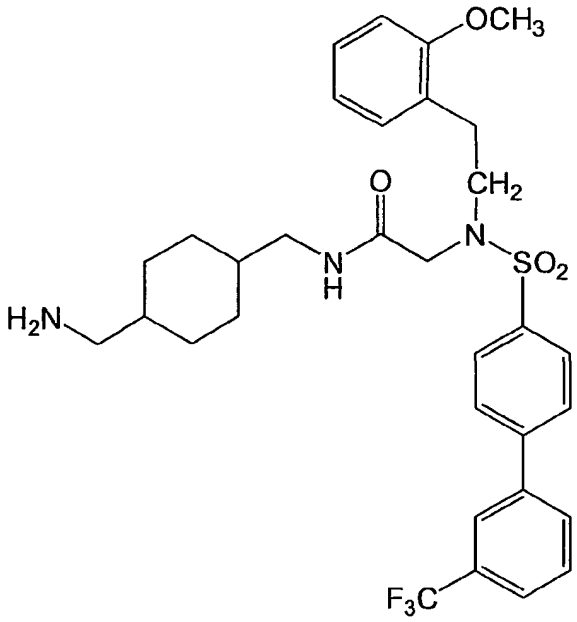
F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 373-377 were prepared according to the procedure above with suitable selection and substitution of a suitably substituted benzeneboronic acid in Step E.

EXAMPLE 8

COMPOUND #29



A. Preparation of Amino Carbamate resin.

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,4-cyclohexylmethylamine (5.69 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic acid.

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the secondary amine

(Displacement of bromide by 2-(2-methoxy)phenethylamine)

The 2-bromoacetylated resin (from B) was swelled in DMSO (approximately 150 ml). To the suspension was added 2-(2-methoxy)phenethylamine (6.045 g, 40 millimoles) and shaken overnight. The

resin was filtered and washed with 3 portions of DMSO, 3 portions methanol, 3 portions DCM/5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

D. Preparation of bromophenylsulfonamide Resin

The resin-bound secondary amine (from C) was swelled in DCM (approximately 200 ml). To the suspension was added pyridine (3.19 g) followed by 4-bromophenylsulfonylchloride (5.1 g, 20 millimoles) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Sulfonamide Resin

The 4-bromophenylsolfonamide resin (from D) was split into 30 portions, each containing 0.133 millimoles of resin. To one portion was added 3-trifluorobenzeneboronic acid (0.076 g, 0.399 millimoles). To the solution was then added palladium tetrakistriphenylphosphine (0.0154 g, 0.133 millimoles), DME (2.5 ml) and 2M sodium carbonate solution in water (0.830 ml). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

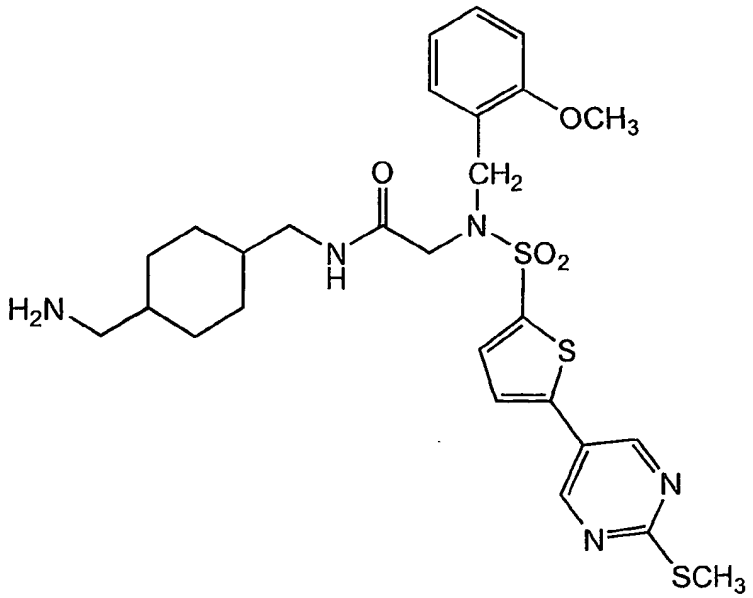
F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 1-9, 20-28 and 30-38 were prepared according to the procedure above with appropriate selection and substitution of methoxybenzylamine or methoxyphenethylamine in Step C above, and appropriate selection and substitution of a suitably substituted benzeneboronic acid in Step E above.

EXAMPLE 9

COMPOUND #73



A. Preparation of Amino Carbamate Resin

Wang p-nitrophenylcarbonate resin (4.0 millimole) was swelled in DMF (200 mL). To the suspension was added 1,4-cyclohexylmethylamine (5.69 g, 40.0 millimole) dissolved in DMF (75 mL). The mixture was shaken for 24 hours. The solvent was removed by filtration. The resin was washed with 3 portions of DMF, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3 portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added 2-methoxybenzylamine (5.226 mL, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3

portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of Sulfonamide Resin

The resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) followed by 5-bromo-2-thiophenesulfonyl chloride (5.23 g, 20.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Substituted Phenylsulfonamide Resin

The 4-bromophenylsulfonamide resin (from D) was split into 23 portions, each containing 0.174 millimole of resin. To one portion was added 5-(2-methylthiopyrimidyl)boronic acid (0.089 g, 0.522 millimole). To the solution was then added palladium tetrakistriphenylphosphine (0.020, 0.0174 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (1.086 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

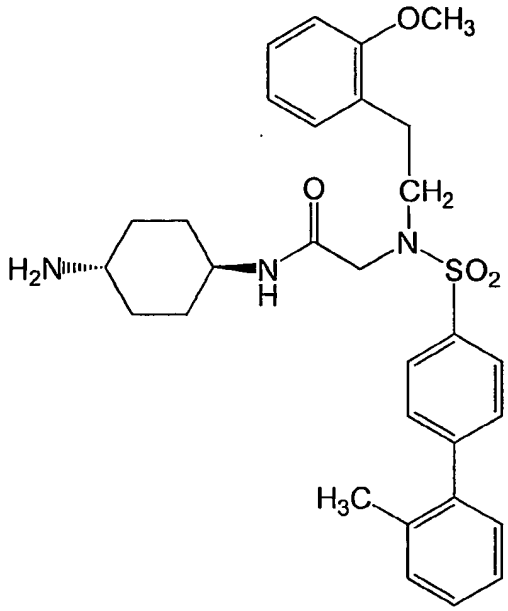
F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 39-72 were similarly prepared according to the procedure above with appropriate selection and substitution of suitably substituted bromo-sulfonyl chloride in Step C above, and appropriate selection and substitution of a suitably substituted benzeneboronic acid in Step E above.

EXAMPLE 10

COMPOUND #94



A. Preparation of Amino Carbamate resin.

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added trans-1,4-bisaminocyclohexane (4.57 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic acid.

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the secondary amine

(Displacement of bromide by 2-(2-methoxy)phenethylamine)

The 2-bromoacetylated resin (from B) was swelled in DMSO (approximately 150 ml). To the suspension was added 2-(2-methoxy)phenethylamine (6.045 g, 40 millimoles) and shaken overnight. The

resin was filtered and washed with 3 portions of DMSO, 3 portions methanol, 3 portions DCM/5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

D. Preparation of bromophenylsulfonamide Resin

The resin-bound secondary amine (from C) was swelled in DCM (approximately 200 ml). To the suspension was added pyridine (3.19 g) followed by 4-bromophenylsulfonylchloride (5.1 g, 20 millimoles) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Sulfonamide Resin

The 4-bromophenylsolfonamide resin (from D) was split into 30 portions, each containing 0.133 millimoles of resin. To one portion was added 2-methylbenzeneboronic acid (0.054 g, 0.399 millimoles). To the solution was then added palladium tetrakistriphenylphosphine (0.0154 g, 0.133 millimoles), DME (2.5 ml) and 2M sodium carbonate solution in water (0.830 ml). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

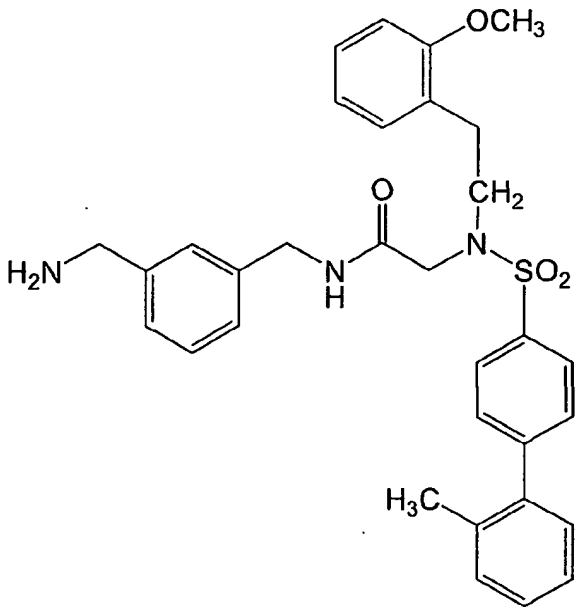
F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 74-93 and 95-113 were prepared according to the procedure above with appropriate selection and substitution 2-methoxyphenethylamine or 2-methoxybenzylamine in Step C above and appropriate selection and substitution of a suitably substituted boronic acid in Step E above.

EXAMPLE 11

COMPOUND #344



A. Preparation of Amino Carbamate Resin

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,3-xylenediamine (5.44 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid , 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added 2-methoxyphenethylamine (5.226 mL, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3

portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Bromophenylsulfonamide Resin

The resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) followed by 4-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Substituted Phenylsulfonamide Resin

The 4-bromophenylsulfonamide resin (from D) was split into 23 portions, each containing 0.174 millimole of resin. To one portion was added 2-methylbenzeneboronic acid (0.071 g, 0.522 millimole). To the solution was then added palladium tetrakistriphenylphosphine (0.020, 0.0174 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (1.086 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

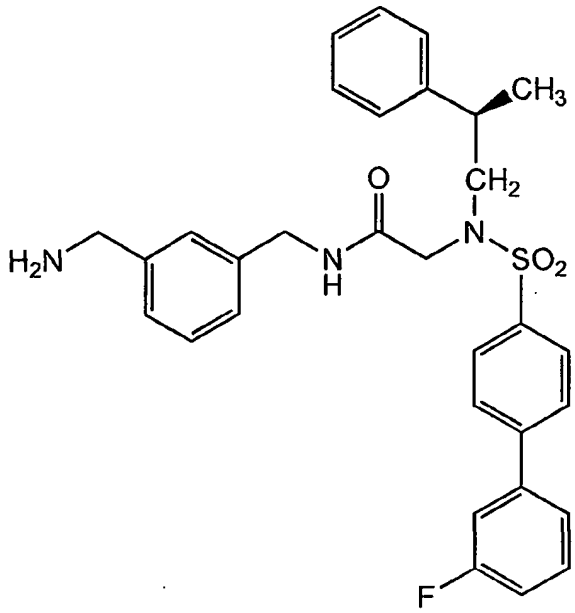
F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 345-351 were prepared according to the procedure above with appropriate selection and substitution of methoxybenzylamine or methoxyphenethylamine in Step C above and appropriate selection and substitution of a suitably substituted benzeneboronic acid in Step E above.

EXAMPLE 12

COMPOUND #392



A. Preparation of Amino Carbamate resin

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,3-xylenediamine (5.44 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid , 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Optically Pure Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added (R)-β-methylphenethylamine (5.408 g, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3

portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Bromophenylsulfonamide Resin

The optically pure resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) and then 4-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole). The suspension was shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Sulfonamide Resin

The N-(R)-β-methylphenthyl-4-bromophenyl-sulfonamide resin (from D) was split into 10 portions, each containing 0.133 millimole of resin. To one portion was 3-fluorobenzeneboronic acid (0.056 g, 0.399 millimoles). To the solution was then added palladium tetrakistriphenylphosphine (0.0154, 0.0133 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (0.830 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

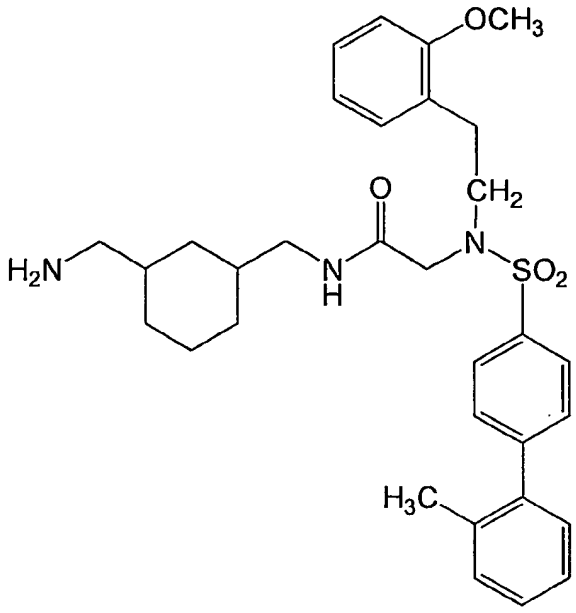
F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 390, 391, 393, 394 and 395 were prepared according to the procedure above with appropriate selection and substitution of a suitably substituted boronic acid in Step E.

EXAMPLE 13

COMPOUND #336



A. Preparation of Amino Carbamate Resin

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,3-bisaminomethylcyclohexane (5.69 g, 40 mmol) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added 2-methoxybenzylamine (5.226 mL, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3

portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Bromophenylsulfonamide Resin

The resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) followed by 4-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Substituted Phenylsulfonamide Resin

The 4-bromophenylsulfonamide resin (from D) was split into 23 portions, each containing 0.174 millimole of resin. To one portion was added 2-methylbenzeneboronic acid (0.071 g, 0.522 millimole). To the solution was then added palladium tetrakistriphenylphosphine (0.020, 0.0174 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (1.086 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

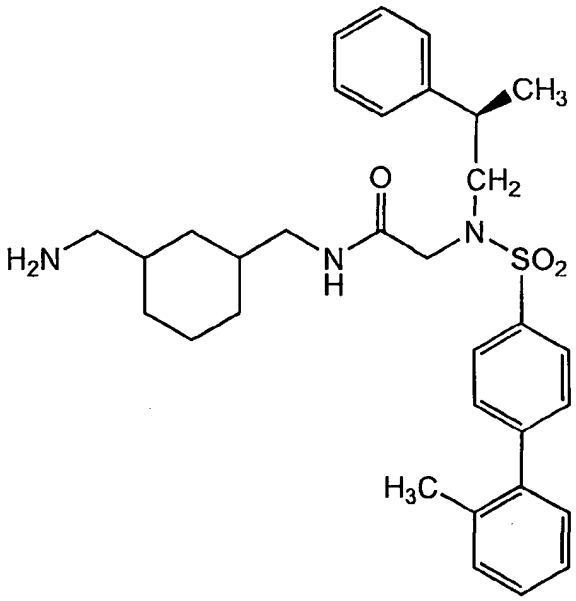
F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 337-343 were similarly prepared according to the procedure above with suitable selection and substitution of a suitably substituted benzeneboronic acid in Step E.

EXAMPLE 14

COMPOUND #384



A. Preparation of Amino Carbamate resin

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,3-bisaminomethylcyclohexane (5.69 g, 40 mmol) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid , 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Optically Pure Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added (R)-β-methylphenethylamine (5.408 g, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3

portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Bromophenylsulfonamide Resin

The optically pure resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) and then 4-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole). The suspension was shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Substituted Phenylsulfonamide Resin

The N-(R)-β-methylphenethyl-4-bromophenyl-sulfonamide resin (from D) was split into 10 portions, each containing 0.133 millimole of resin. To one portion was 2-methylbenzeneboronic acid (0.054 g, 0.399 mmol). To the solution was then added palladium tetrakistriphenylphosphine (0.0154, 0.0133 millimole), DME (2.5 mL) and 2M sodium carbonate solution in water (0.830 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

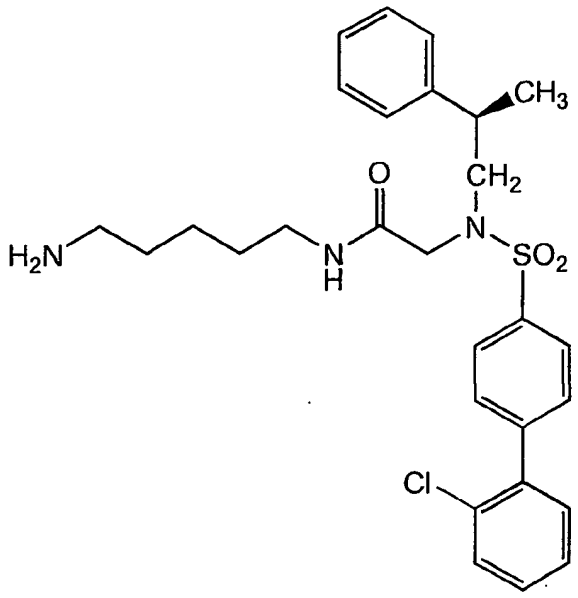
F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 385-389 were similarly prepared according to the procedure above, by appropriate selection of optically pure methylphenethylamine in Step C above, and appropriate selection and substitution of a suitably substituted boronic acid in Step E.

EXAMPLE 15

COMPOUND #379



A. Preparation of Amino Carbamate resin

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 15-pentanediamine (4.09 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid , 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Optically Pure Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added (R)-β-methylphenethylamine (5.408 g, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3

portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Bromophenylsulfonamide Resin

The optically pure resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) and then 4-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole). The suspension was shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Sulfonamide Resin

The N-(R)-β-methylphenthyl-4-bromophenyl-sulfonamide resin (from D) was split into 10 portions, each containing 0.133 millimole of resin. To one portion was 2-chlorobenzeneboronic acid (0.076 g, 0.399 millimole). To the solution was then added palladium tetrakistriphenylphosphine (0.0154, 0.0133 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (0.830 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

F. Cleavage of the Resin Support

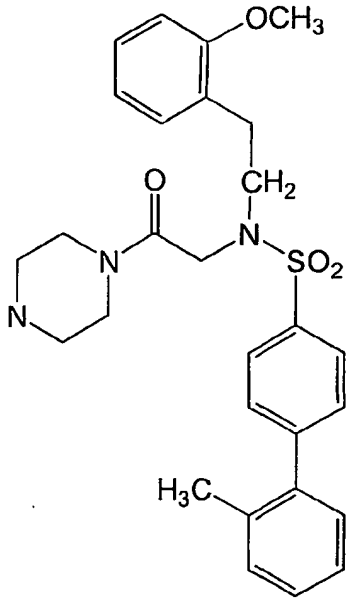
The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 352, 378 and 380-383 were prepared according to the procedure above with appropriate selection and substitution of substituted benzeneboronic acid in Step E.

Compounds 353-359 and 396-401 were similarly prepared according to the procedure above with substitution of 1,6-n-hexyl diamine for the 1,5-n-pentyl diamine in step B and appropriate selection and substitution of suitably substituted benzeneboronic acid in Step E.

EXAMPLE 16

COMPOUND #151



A. Preparation of Piperazino Carbamate Resin

Wang p-nitrophenylcarbonate resin (4.0 millimole) was swelled in DMF (200 mL). To the suspension was added piperazine (3.446 g, 40.0 millimole) dissolved in DMF (75 mL). The mixture was shaken for 24 hours. The solvent was removed by filtration. The resin was washed with 3 portions of DMF, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3 portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added 2-methoxybenzylamine (5.226 mL, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3

portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Bromophenylsulfonamide Resin

The resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) followed by 4-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Substituted Phenylsulfonamide Resin

The 4-bromophenylsulfonamide resin (from D) was split into 23 portions, each containing 0.174 millimole of resin. To one portion was added 2-methylbenzeneboronic acid (0.071 g, 0.522 millimole). To the solution was then added palladium tetrakistriphenylphosphine (0.020, 0.0174 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (1.086 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

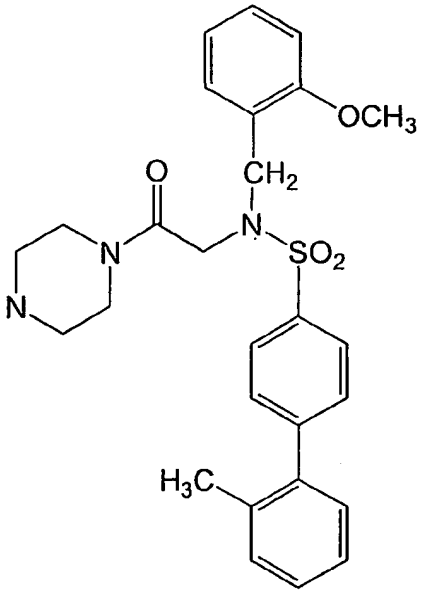
F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 152-173 were prepared according to the procedure above with appropriate selection and substitution of substituted boronic acid in step E.

EXAMPLE 17

COMPOUND #174



A. Preparation of Piperazino Carbamate Resin

Wang p-nitrophenylcarbonate resin (4.0 millimole) was swelled in DMF (200 mL). To the suspension was added piperazine (3.446 g, 40.0 millimole) dissolved in DMF (75 mL). The mixture was shaken for 24 hours. The solvent was removed by filtration. The resin was washed with 3 portions of DMF, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3 portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added 2-methoxybenzylamine (5.226 mL, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3

portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Bromophenylsulfonamide Resin

The resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) followed by 4-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Substituted Phenylsulfonamide Resin

The 4-bromophenylsulfonamide resin (from D) was split into 23 portions, each containing 0.174 millimole of resin. To one portion was added 2-methylbenzeneboronic acid (0.071 g, 0.522 millimole). To the solution was then added palladium tetrakistriphenylphosphine (0.020, 0.0174 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (1.086 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

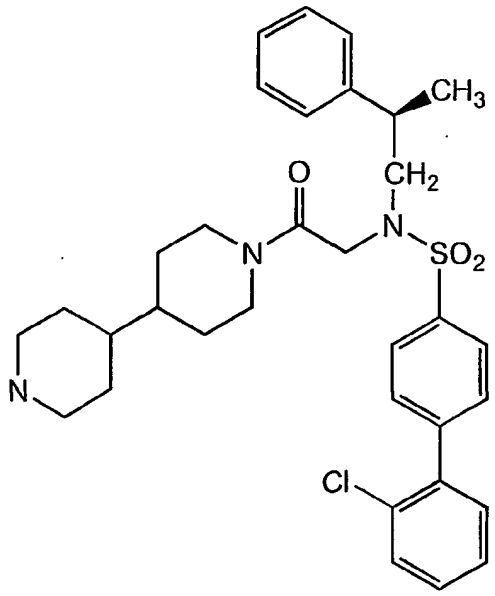
F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 175-196 were prepared according to the procedure above with appropriate selection and substitution of substituted boronic acid in step E.

EXAMPLE 18

COMPOUND #367



A. Preparation of Bipiperidino resin

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 4,4'-bipiperdine (6.73 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid , 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Optically Pure Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added (R)-β-methylphenethylamine (5.408 g, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3

portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Bromophenylsulfonamide Resin

The optically pure resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) and then 4-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole). The suspension was shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Sulfonamide Resin

The N-(R)-β-methylphenthyl-4-bromophenyl-sulfonamide resin (from D) was split into 10 portions, each containing 0.133 millimole of resin. To one portion was 2-chlorobenzeneboronic acid (0.076 g, 0.399 millimole). To the solution was then added palladium tetrakistriphenylphosphine (0.0154, 0.0133 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (0.830 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

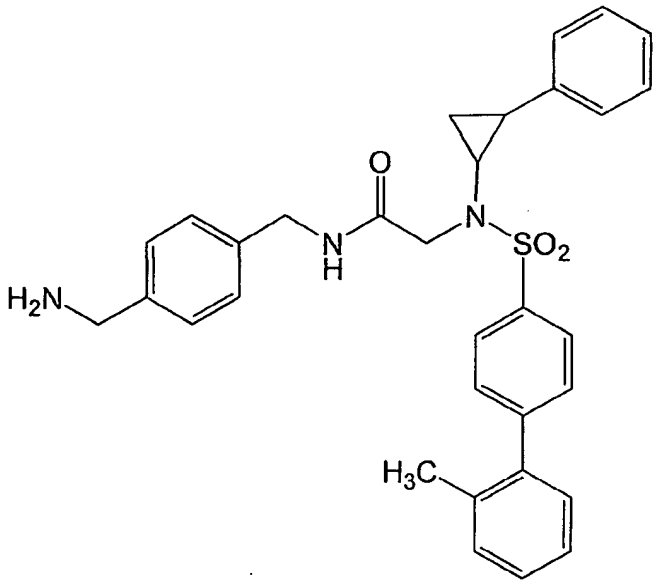
F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 366 and 368-371 were prepared according to the procedure above with appropriate selection and substitution optically pure methylphenethylamine in Step C and appropriate selection and substitution of a suitably substituted benzeneboronic acid in Step E.

EXAMPLE 19

COMPOUND #320



A. Preparation of Amino Carbamate resin

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,4-xylenediamine (5.44 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid , 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added 1-amino-2-phenyl-cyclopropane (5.33 g, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3

portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Bromophenylsulfonamide Resin

The optically pure resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) and then 4-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole). The suspension was shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Sulfonamide Resin

The 4-bromophenyl-sulfonamide resin (from D) was split into 10 portions, each containing 0.133 millimole of resin. To one portion was 2-methylbenzeneboronic acid (0.076 g, 0.399 millimole). To the solution was then added palladium tetrakistriphenylphosphine (0.0154, 0.0133 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (0.830 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

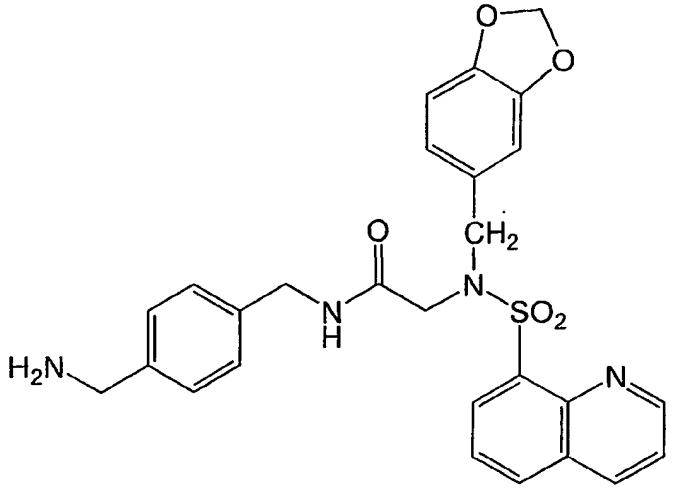
F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 321 and 322 were prepared according to the above procedure with appropriate selection and substitution of a suitably substituted benzeneboronic acid in Step E.

EXAMPLE 20

COMPOUND #405



A. Preparation of Amino Carbamate Resin.

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,4-xylenediamine (5.44 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid , 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic acid.

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the secondary amine

(Displacement of bromide by 2-methoxybenzylamine)

The 2-bromoacetylated resin (from B) was swelled in DMSO (approximately 150 ml). To the suspension was added 3,4-methylenedioxy-benzylamine (6.05 g, 40 millimoles) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions methanol, 3 portions

DCM/5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

D. Preparation of Sulfonamide Resin

The resin bound secondary amine (from C) was split into 36 portions each containing 0.111 millimole of resin. One portion was swelled in DCM (1.5 ml). To the suspension was added pyridine (0.089 g), followed by 8-quinolinylsulfonyl chloride (9.70 g, 0.556 millimoles) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

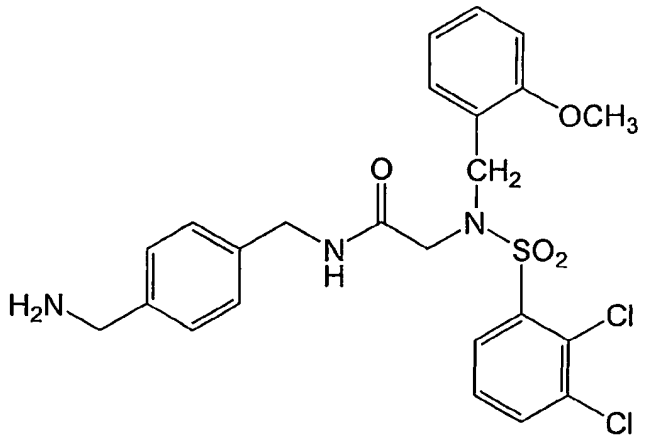
E. Cleavage of the Resin Support

The product was cleaved from the resin using a cleaving cocktail solution of 90:10 TFA:water. The cleavage solution was evaporated. The product was purified by semi-preparative reversed phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product wa lyophilized and analyzed by ES/MS and reversed phase HPLC.

Compounds 403, 408, 409 and 411 were prepared according the above procedure with appropriate selection and substitution of a suitable diamine in Step A.

EXAMPLE 21

COMPOUND #404



A. Preparation of Amino Carbamate Resin.

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,4-xylenediamine (5.44 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic acid.

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the secondary amine

(Displacement of bromide by 2-methoxybenzylamine)

The 2-bromoacetylated resin (from B) was swelled in DMSO (approximately 150 ml). To the suspension was added 2-methoxybenzylamine (5.226 mL g, 40 millimoles) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions methanol, 3 portions DCM/5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

D. Preparation of Sulfonamide Resin

The resin bound secondary amine (from C) was split into 36 portions each containing 0.111 millimole of resin. One portion was swelled in DCM (1.5 ml). To the suspension was added pyridine (0.089 g), followed by 2,3-dichlorobenzene sulfonyl chloride (0.137g, 0.556 millimoles) and shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Cleavage of the Resin Support

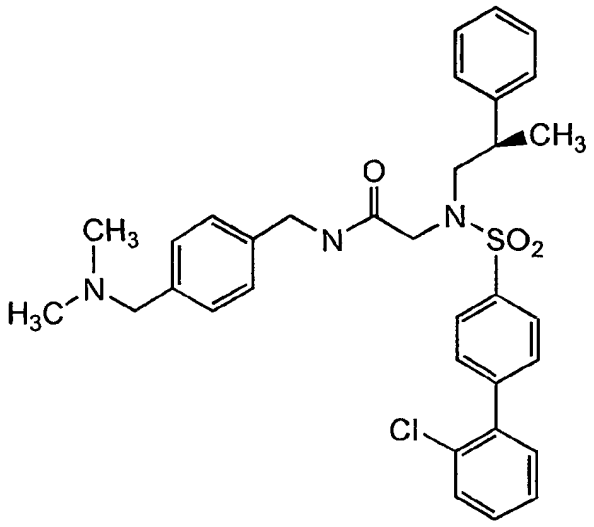
The product was cleaved from the resin using a cleaving cocktail solution of 90:10 TFA:water. The cleavage solution was evaporated. The product was purified by semi-preparative reversed phase HPLC on a 20X100

mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product wa lyophilized and analyzed by ES/MS and reversed phase HPLC.

Compounds 402, 406, 407 and 410 were prepared according the above procedure with appropriate selection and substitution of a suitable diamine in Step A.

Example 22

COMPOUND #471



A. Dimethylation of Compound #198.

Compound #198, prepared as in Example 1 (100 mg, 0.178 millimoles) was dissolved in an equal mixture of TMOF and DCE (3.0 mL). To the solution were then added formaldehyde (16 mg, 0.534 millimoles), $NaBH_3CN$ (34 mg, .534 millimoles), and acetic acid (45 μL, 1.5 %). The mixture was stirred for 16h, and then the reaction was stopped by adding water. The crude product was extracted with chloroform, and the solvent removed under vacuum, to yield the product.

B. Purification of product.

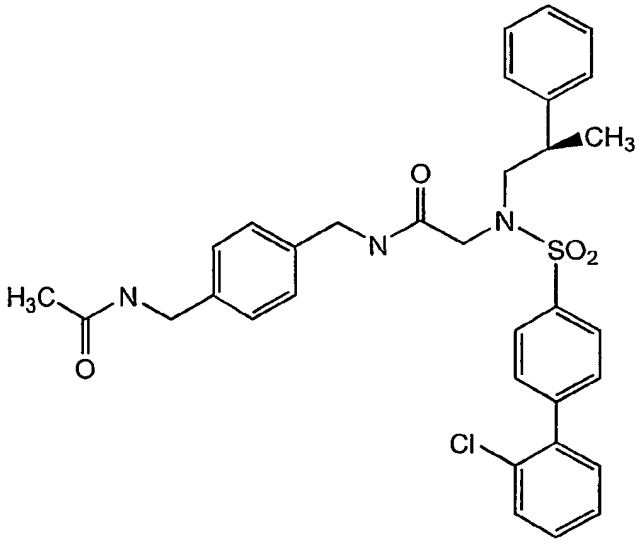
The crude product prepared in Step A was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0:0.1 water:acetonitrile:TFA to 10:90:0.1

water:acetonitrile:TFA. The product was lyophillized and analyzed by ES^+/MS and reverse phase HPLC.

Compounds 472, 474, 475 were similarly prepared according to the procedure above with appropriate selection and substitution of reagents (Compound 472 was prepared by replacing the formaldehyde in Step A with acetaldehyde; Compound 474 was prepared by replacing compound 198 in Step A with compound 215; and Compound 475 by substituting compound 198 and formaldehde were in Step A with compound 215 and acetaldehyde, respectively).

Example 23

COMPOUND #473



A. Acetylation of Compound # 198.

Compound #198, prepared as in Example 1, (100 mg, 0.178 millimoles) was dissolved in chloroform (3.0 mL). To the solution were added acetyl chloride (19 45 μL, 0.267 millimoles), and TEA (37 45 μL, 0.267 millimoles), and the mixture stirred for 16. The reaction was then stopped by adding water. The crude product was washed twice by 10% $NaHCO_3$ aqueous solution.

B. Purification of product.

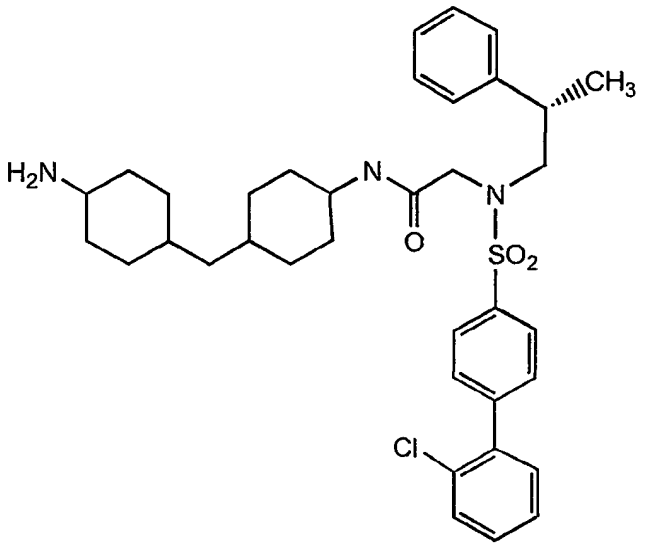
The crude product from Step A was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of

90:10:0:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES^+/MS and reverse phase HPLC.

Compound 476 was similarly prepared according to the procedure above, with substitution of compound 198 in Step A with compound 215.

Example 24

Compound #497



A. Preparation of Amino Carbamate resin

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 4,4-methylenebis(cyclohexanamine) (8.41 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from Step A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and the mixture shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Optically Pure Secondary Amine on Resin

The 2-bromoacetylated resin (from Step B) was swelled in DMSO (150 mL). To the suspension was added (R)-β-methylphenethylamine (5.408 g, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3 portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Bromophenylsulfonamide Resin

The optically pure resin-bound secondary amine resin (from Step C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) and then 4-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole). The suspension was shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Sulfonamide Resin

The N-(R)-β-methylphenthyl-4-bromophenyl-sulfonamide resin (from Step D) was split into 10 portions, each containing 0.133 millimole of resin. To one portion was added 2-chlorobenzeneboronic acid (0.076 g, 0.399 millimole). To the solution were then added palladium tetrakistriphenylphosphine (0.0154, 0.0133 millimole), DME (2.5 mL) and 2M sodium carbonate solution in water (0.830 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

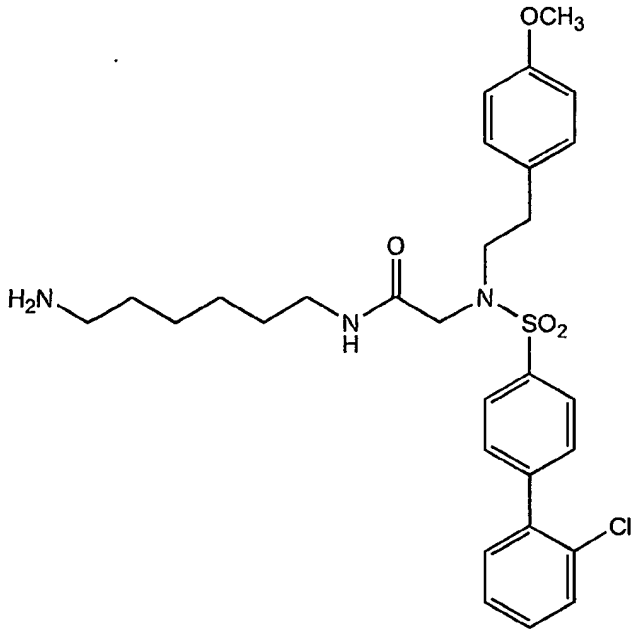
F. Cleavage of the Resin Support

The product from Step E was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 498 through 501 were similarly prepared according to the procedure above with appropriate selection and substitution the desired optically pure phenethylamine in Step C and appropriate selection and substitution of suitably substituted benzeneboronic acid in Step E.

EXAMPLE 25

COMPOUND # 502



A. Preparation of Amino Carbamate resin

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,6-hexanediamine (4.65 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from Step A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Secondary Amine on Resin

The 2-bromoacetylated resin (from Step B) was swelled in DMSO (150 mL). To the suspension was added 4-methoxyphenethylamine (6.05 g, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3

portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3 portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Bromophenylsulfonamide Resin

The optically pure resin-bound secondary amine resin (from Step C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) and then 4-bromophenylsulfonyl chloride (5.1 g, 20.0 millimole). The suspension was shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Sulfonamide Resin

The N-(R)-β-methylphenthyl-4-bromophenyl-sulfonamide resin (from Step D) was split into 10 portions, each containing 0.133 millimole of resin. To one portion was added 2-chlorobenzeneboronic acid (0.076 g, 0.399 millimole). To the solution was then added palladium tetrakistriphenylphosphine (0.0154, 0.0133 millimole), DME (2.5 mL) and 2M sodium carbonate solution in water (0.830 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

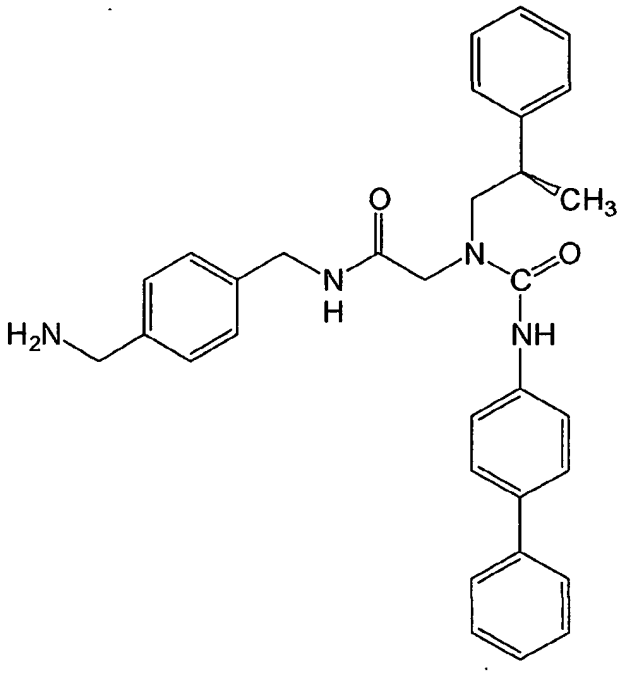
F. Cleavage of the Resin Support

The product from Step E was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 501 through 515 and 572 through 589 may be similarly prepared according to the procedure above with suitably substituted phenethylamines in Step C.

EXAMPLE 26

COMPOUND #590



A. Preparation of Amino Carbamate resin

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 1,4-xylenediamine (5.44 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from Step A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Optically Pure Secondary Amine on Resin

The 2-bromoacetylated resin (from Step B) was swelled in DMSO (150 mL). To the suspension was added (R)-β-methylphenethylamine (5.408 g, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3

portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Biphenylurea Resin

The optically pure resin-bound secondary amine resin from Step C (0.150 mmol) was swelled in DCE (2.0 mL). To the suspension was added 4-biphenylisocyanate (0.146 g, 0.750 mmol). The suspension was shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

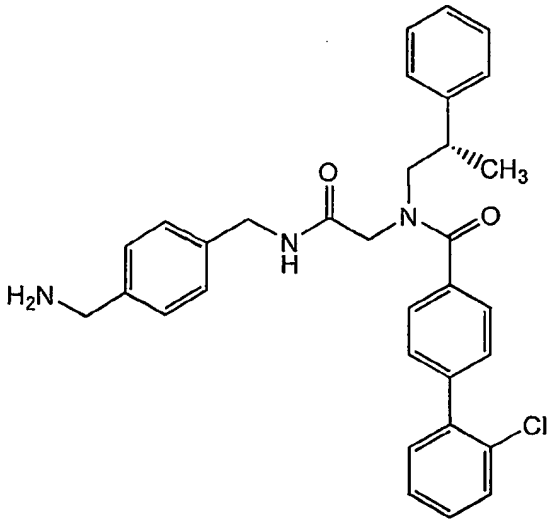
E. Cleavage of the Resin Support

The product from Step D was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compound #591 was similarly prepared according to the procedure described above with appropriate substitution of (S)-β-methylphenethylamine in Step C.

Example 27

Compound # 477



A. Preparation of Amino Carbamate resin

Wang p-nitrophenylcarbonate resin (4.0 millimoles) was swelled in DMF (approximately 200 ml). To the suspension was added 4,4-methylenebis(cyclohexanamine) (8.41 g, 40 millimoles) dissolved in DMF (75 ml). The mixture was shaken for 24h. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, 3 portions DCM/ 5% acetic acid, 3 portions methanol, 3 portions DCM/10% TEA, and 3 portions methanol. The resin was dried *in vacuo* overnight.

B. Coupling of Bromoacetic Acid

The carbamate resin (from A) was swelled in DMF (approximately 200 ml). To the suspension was added bromoacetic acid (2.77 g, 20 millimoles) and diisopropylcarbodiimide (2.53 g) and shaken overnight. The solvent was removed by filtration. The resin was then washed with 3 portions DMF, 3 portions methanol, and 3 portions DCM.

C. Preparation of the Optically Pure Secondary Amine on Resin

The 2-bromoacetylated resin (from B) was swelled in DMSO (150 mL). To the suspension was added (R)-β-methylphenethylamine (5.408 g, 40.0 millimole) and shaken overnight. The resin was filtered and washed with 3 portions of DMSO, 3 portions of methanol, 3 portions of DCM/ 5% acetic acid, 3 portions of methanol, 3 portions of DCM/ 10% TEA, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

D. Preparation of 4-Iodobenzamide Resin

The optically pure resin-bound secondary amine resin (from C) was swelled in DCM (200 mL). To the suspension was added pyridine (3.19 g) and then 4-iodobenzoyl chloride (5.3 g, 20.0 millimole). The suspension was shaken overnight. The resin was filtered and washed with 3 portions of DCM, 3 portions of methanol, 3 portions of DCM, and 3 portions of methanol. The resin was dried *in vacuo* overnight.

E. Preparation of Sulfonamide Resin

Five portions of the N-(R)-β-methylphenthyl-4-iodobenzamide resin (from D), each containing 0.133 millimole of resin, were used for the next reaction. To one portion was added 2-chlorobenzeneboronic acid (0.076 g, 0.399 millimole). To the solution was then added palladium

tetrakistriphenylphosphine (0.0154, 0.0133 millimole), DME (2.5 mL) and 2 M sodium carbonate solution in water (0.830 mL). The mixture was shaken at 80°C overnight. The resin was filtered and washed with 3 portions DMF, 3 portions methanol and 3 portions DCM. The resin was dried *in vacuo* overnight.

F. Cleavage of the Resin Support

The product was cleaved from the resin with a solution of 90:10 TFA/water. The cleavage solution was evaporated. The product was purified by semi-preparative reverse phase HPLC on a 20X100 mm J'sphere H-80 YMC column using a gradient of 90:10:0.1 water:acetonitrile:TFA to 10:90:0.1 water:acetonitrile:TFA. The product was lyophillized and analyzed by ES/MS and reverse phase HPLC.

Compounds 478-481 were similarly prepared according to the procedure above, with appropriate selection and substitution of suitably substituted benzeneboronic acid in Step E.

EXAMPLE 28

IN VITRO TESTING: hFSH-R CHO Cells

Preparation of Biological Materials

Minimum Essential Medium-Alpha (MEM-alpha), fetal bovine serum (FBS), penicillin, streptomycin, geneticin, trypsin-EDTA, Hanks' Balanced Salt Solution (no Calcium chloride, Magnesium chloride, Magnesium sulfate, or phenol red; Ca-Mg free HBSS) were purchased from Gibco BRL (Gaithersburg, MD). The cells used for the FSH bioassay (rhFSHR-cLUC) were Chinese Hamster Ovary cells (K-1; ATCC) stably transformed with human FSH receptor (pSVK-FSHr) and a cAMP luciferase reporter gene (responsive CGα-180LUC). Follicle Stimulating Hormone (Metrodin; Fertinex) was purchased from Serono, Ltd. (Norwell, MA).

The rhFSHR-cLUC cell cultures were maintained in MEM-Alpha supplemented with 10% heat-inactivated FBS (HIFBS), 100 U/ml penicillin, 100 µg/mL streptomycin, and included 0.1 g/L geneticin for stable cell selection.

HFSHR Assay Procedure

Forty-eight hours after the cells were plated in sterile 96-well culture plates (Corning, Corning, NY) the spent media was removed and 50 µl assay media (modified growth media with 2% HIFBS) containing 2mM IBMX (3-isobutyl-1-methyl-xanthine) was added to the cells. Compounds (25 µl) in the appropriate concentration were added followed 5 minutes later by an EC_{70} dose of FSH (25 µl; 160 ng/ml; 4.85 nM). After 10 minutes @ 22.5°C (room temperature) the reaction was terminated by addition of 25 µL 0.5 N hydrochloric acid to each well. The amount of cAMP produced was measured by radioimmunoassay in a FlashPlate (DuPont, Boston, MA). To each flash plate 60 µL flash plate buffer was added followed by 40 µL acidified cell sample or cAMP standard, followed with the addition of 100 µl ^{125}I-cAMP trace. The FlashPlates were sealed, incubated overnight @ room temperature, and counted in a Packard TopCount (Packard Instrument Co., Meriden, CT). The cAMP radioimmunoassay results were calculated using DPM conversion and log-logit transformation of % binding (Excel program).

Preparation of Test Compound

Test compounds were solubilized in 30% dimethyl sulfoxide (DMSO) at a concentration of 10 mM before diluting to appropriate concentrations in assay medium. The final DMSO concentration in the treated cells and in the control cells was 0.75%. The compounds were tested in the assay at a maximum final concentration of 50 µM (primary assay) and compounds that demonstrated greater than 50% inhibition or greater than 200% stimulation of cAMP production were retested in dose-ranging experiments to calculate an EC_{50}.

Derivation and Analysis of Data

For individual experiments, a set of samples were tested including a vehicle control (assay buffer), a reference compound (hFSH) at a range of concentrations designed to elicit a minimal to maximal response, and several

concentrations of test compounds together with an EC_{70} concentration of standard (hFSH challenge). Each compound was performed in duplicates for the primary evaluation and quadruplicates for the dose-ranging experiments. The cAMP radioimmunoassay raw data (pmol) were calculated to provide average pmol cAMP produced/ml and the percent inhibition was calculated as shown below.

$$\% \text{ Inh} = [1 - (\text{Avg. pmol}_{\text{test compound+standard}}) / (\text{Avg. pmol}_{\text{standard}})] \times 100$$

EC_{50} values were calculated from an analysis of the concentration-inhibition data using a linear analysis of the data transformed to a log-logit format.

TABLE 5

Cmpd #	EC_{50} hFSHR CHO cAMP (μM)	Cmpd #	EC_{50} hFSHR CHO-cAMP (μM)
1	1.16	278	1.09
2	0.93	279	2.45
3	0.6	280	7.63
4	0.65	281	6.95
5	0.96	282	9.4
6	1.59	283	1.27
7	1.81	284	3.51
8	1.38	285	7.89
9	1.06	286	3.88
10	3.71	287	7.52
11	0.63	288	19.51
12	0.68	289	5.68
13	0.56	290	0.67
14	0.74	291	8.94
15	0.84	292	0.68
16	1.13	293	7.36
17	0.57	294	1.54

	18	1.82	295	2.18
	19	3.37	296	50
	20	6.31	297	6.88
	21	3.29	298	34.38
5	22	5.03	299	2.22
	23	1.41	300	3.18
	24	2.33	301	0.15
	25	1.41	302	0.2
	26	1.46	303	0.44
10	27	2.3	304	0.3
	28	2.23	305	0.58
	29	3.09	306	0.35
	30	1.33	307	0.19
	31	0.91	308	0.45
15	32	0.31	309	0.34
	33	0.42	310	0.22
	34	0.31	311	0.05
	35	0.83	312	0.22
	36	0.66	313	0.43
20	37	0.67	314	0.69
	38	0.5	315	0.31
	39	1.69	316	0.96
	40	22.13	317	16.92
	41	12.69	318	16.97
25	42	6.46	319	1.1
	43	9.88	320	2.57
	44	8.92	321	11.3
	45	3.92	322	4.36
	46	28.85	323	0.29
30	47	4.37	324	0.37
	48	3.62	325	16.96
	49	31.3	336	0.98
	50	26.24	337	0.31

	51	25	338	0.44
	52	28.49	339	1.1
	53	29.02	340	0.65
	54	33.45	341	0.57
5	55	50	342	0.37
	56	23.32	343	0.53
	57	19.52	344	0.7
	58	6.24	345	18.22
	59	28.48	346	0.65
10	60	40.02	347	0.9
	61	50	348	2.24
	62	6.76	349	0.79
	63	33.61	350	17.47
	64	38.47	351	3.15
15	65	4.82	352	0.11
	66	12.67	353	0.14
	67	50	354	0.37
	68	37.66	355	0.4
	69	5.99	356	0.89
20	70	18.78	357	0.3
	71	11	358	1.04
	72	7.85	359	0.36
	73	4.95	366	0.78
	74	10.68	367	1.02
25	75	5.09	368	1.08
	76	10.21	369	0.75
	77	6.86	370	0.57
	78	12.87	371	1.84
	79	7.83	372	0.19
30	80	3.06	373	0.11
	81	7.06	374	0.34
	82	5.09	375	0.13
	83	4.5	376	0.17

	84	50	377	0.34
	85	7.79	378	0.25
	86	12.34	379	50
	87	7.4	380	1.2
5	88	12.2	381	0.45
	89	50	382	0.61
	90	50	383	2.9
	91	13.19	384	0.27
	92	50	385	0.33
10	93	15.22	386	1.17
	94	34.45	387	1.07
	95	5.98	388	0.9
	96	8.23	389	1.93
	97	4.31	390	0.23
15	98	6.04	391	0.31
	99	3.68	392	0.26
	100	4.99	393	0.09
	101	4.89	394	0.72
	102	3.98	395	2.64
20	103	28.32	396	0.09
	104	9.54	397	0.05
	105	31.33	398	0.22
	106	12.77	399	0.23
	107	9.7	400	0.16
25	108	5.5	401	1.36
	109	4.76	402	5.36
	110	10.75	412	0.32
	111	8.39	413	0.08
	112	10.21	414	0.35
30	113	16.69	415	0.72
	114	9.78	416	0.51
	115	2.92	417	0.44
	116	8.41	418	0.85

	117	3.63	419	2.07
	118	1.24	420	0.64, 0.21
	119	0.54	421	0.55
	120	1.5	422	0.52
5	121	33.11	423	1.38
	122	0.76	424	18.85
	123	4.03	425	0.42
	124	1.11	426	0.7
	125	7.53	427	4.75
10	126	2.31	428	>50
	127	10.36	429	3.03, 0.77
	128	4.98	430	>50
	129	2.11	431	5.98
	130	1.86	432	>50
15	131	1.41	433	23.5
	132	2.58	434	0.2
	133	50	435	0.21
	134	3.86	436	50
	135	1.02	437	32.5
20	136	2.13	438	0.73
	137	4.32	439	>50
	138	31.21	440	0.9
	139	5.76	441	0.12
	140	18.57	442	>50
25	141	50	443	0.85
	142	50	444	1.89
	143	5	445	1.54
	144	1.08	446	>50
	145	24.26	447	>50
30	146	1.73	448	>50
	147	8.06	449	0.64
	148	23.5	450	0.21
	149	1.01	451	0.29, 0.52

	150	4.53	452	0.58
	151	9.79	453	0.37
	152	8.58	454	0.86
	153	9.44	455	0.23
5	154	10.68	456	3.35
	155	12.64	457	0.58
	156	20.37	458	20.9
	157	10.27	459	9.05
	158	8.34	460	0.17
10	159	4.54	461	16.3
	160	28.53	462	1.22
	161	37.9	463	2.14, 0.58
	162	11.24	464	0.73
	163	24.27	465	2.19
15	164	13.8	466	1
	165	12.46	467	0.07
	166	9.09	468	0.51
	167	3.48	469	20.01
	168	24.84	470	50
20	169	8.96	471	49.95
	170	8.66	472	>50
	171	8.99	473	>50
	172	3.76	474	>50
	173	2.23	475	9.46
25	174	50	476	50
	175	47.77	477	7.7
	176	40.59	478	>50
	177	50	479	13.25
	178	50	480	0.62
30	179	50	481	0.67
	180	50	483	0.46
	181	50	484	0.14
	182	50	485	0.11

	183	50	486	2.33
	184	50	487	0.11
	185	50	488	0.22
	186	38.9	489	0.35
5	187	50	490	0.59
	188	50	491	0.11
	189	50	492	1.08
	190	38.23	493	0.99
	191	50	494	0.45
10	192	32.3	495	0.62
	193	50	496	0.13
	194	50	497	4.04
	195	50	498	1.33
	196	50	499	3.46
15	197	0.36	500	2.55
	198	0.04	501	0.79
	199	0.83	502	0.3
	200	0.32	503	0.39
	201	0.41	504	>50
20	202	0.21	505	0.14
	203	0.08	506	1.2
	204	0.54	507	0.08
	205	0.22	508	0.28
	206	0.35	509	0.2
25	207	0.35	510	1.02
	208	0.06	511	0.09
	209	0.77	512	1.37
	210	0.23	513	0.62
	211	0.49	514	0.41
30	212	0.16	515	3.18
	213	0.07	521	0.12
	214	0.15	522	0.41
	215	0.08	523	0.37

	216	0.62	524	0.21
	217	1.2	525	0.76
	218	1.2	526	2.36
	219	1.77	527	0.15
5	220	2.1	528	0.61
	221	5.86	529	0.72
	222	13.52	530	20
	223	6.51	531	>50
	224	9.81	532	21.9
10	225	12.8	533	0.92
	226	5.5	534	1
	227	5.5	535	4.77
	228	3.65	536	>50
	229	3.76	537	0.29
15	230	31.12	538	0.12
	231	5.82	539	4.62
	232	4.46	540	50
	233	8.9	541	0.21
	234	27.85	542	0.1
20	235	8.66	543	0.77
	236	3.13	544	0.82
	237	50	545	0.19
	238	10.49	546	14.8
	239	7.99	547	2.5
25	240	6.83	548	0.23
	241	7.45	549	0.29
	242	3.51	550	0.36
	243	5.17	551	1.27
	244	2.88	552	4.2
30	245	5.63	553	1
	246	4.11	554	0.24
	247	6.27	555	1.93
	248	5.33	556	0.87

	249	6.86	557	0.42
	250	17.11	558	0.41
	251	5.85	559	0.74
	252	8.27	560	0.84
5	253	8.43	561	0.13
	254	4.33	562	3
	255	2.63	563	1.38
	256	2.39	564	0.87
	257	1.64	572	0.13
10	258	2.44	573	0.04
	259	2.98	574	0.21
	260	3.93	575	0.87
	261	5.65	576	0.1
	262	2.46	577	0.14
15	263	31.99	578	50
	264	5.62	579	5.29
	265	2.69	580	0.35
	266	3.43	581	0.1
	267	2.08	582	0.43
20	268	50	583	1.94
	269	6.76	584	0.11
	270	4.19	585	>50
	271	0.96	586	1.24
	272	0.55	587	0.29
25	273	1.16	588	1.06
	274	2.08	589	0.25
	275	1.6	590	2.6
	276	5.1	591	50
	277	31.89		

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EXAMPLE 29

IN VITRO TESTING: Rat Granulosa Cells

Preparation of Biological Materials

Insulin, diethylstilbesterol, androstenedione, forskolin and DMSO were purchased from Sigma (St. Louis, MO). Fungizone, penicillin/streptomycin, charcoal-treated heat inactivated fetal bovine serum (CT-HI-FBS) and Dulbecco's Modified Eagle Medium:Hams F12 medium containing 15 mM Hepes and L-glutamine (DMEM:F12), were purchased from GIBCO BRL (Grand Island, NY).

Ovine FSH (NIADDK-oFSH-17; FSH potency = 20 NIH-FSH-S1 U/mg; LH contamination = 0.04 times NIH-LH-S1) was received from Ogden Bioservices Corporation, Rockville, MD. Human FSH (Fertinex), was purchased from Serono Pharmaceutical (Framingham, MA). Human chorionic gonadotropin (hCG) was purchased from Sigma (St Louis, MO).

Granulosa Cell Culture

Immature intact female rats (Wistar-derived strain; 21 – 23 days old) were implanted with a single pellet (Innovative Research of America, Sarasota, FL) containing 2.5 mg diethylstilbesterol (DES) for 3 days. On the third day, the animals were sacrificed, the ovaries were removed, and the granulosa cells were isolated essentially as described in Haynes-Johnson et al., Biol. Reprod., 61 (1), 147-153, (1999). Granulosa cells were plated at a density of 300,000 cells per ml with 0.2 ml added to each well of 96 well culture dishes (Corning, NY). Cultures were incubated at 37°C in a humidified incubator (95% air, 5% CO2) overnight (18 hours).

For determination of LH-stimulated estrogen production, immature female rats, about 28 days of age, were treated with 75 IU pregnant mares serum gonadotropin (PMSG) and sacrificed 48 hours later. The granulosa cells from large follicles (not corpora lutea) were expressed into media following the procedure outlined above. Granulosa cells were plated at a density of 300,000 cells/ml with 0.2 ml of cell suspension added to each well of a 96-well plate.

Test Procedure

Androstenedione (100,000X) was prepared by dissolving the steroid in 100% ethanol, and was subsequently diluted to a final concentration of 10^{-7}M containing 0.1% ethanol in assay media. The assay media was serum-free, DES-free, insulin-free media, prepared by adding 5 mL pen-strep,1.5 mL fungizone and 5μL androstenedione to 493.5 mL DMEM F-12 media.

Test compounds were solubilized in 30% dimethyl sulfoxide (DMSO) at a concentration of 10 mM before diluting to appropriate concentrations in assay medium. The final DMSO concentration in the treated cells and in the control cells was 0.75%. The compounds were tested in the assay at a maximum final concentration of 50 μM (primary assay) and compounds that demonstrated greater than 50% inhibition or greater than 200% stimulation of cAMP production were retested in dose-ranging experiments to calculate an EC_{50}.

Test plates containing the granulosa cells were preincubated for 18 hours at 37°C with 95% air, 5% CO_2, 100% humidity. The spent media was removed and 50 μl assay media (DMEM:F12) containing 2mM IBMX (3-isobutyl-1-methyl-xanthine) was added to the cells. Compounds (25 μl) in the appropriate concentration were added followed 5 minutes later by an EC_{70} dose of FSH (25 μl; 50 ng/ml; 1.4 nM). After 30 minutes @ 22.5°C (room temperature) the reaction was terminated by addition of 25 μL 0.5 N hydrochloric acid to each well. The amount of cAMP produced was measured by radioimmunoassay in a FlashPlate (DuPont, Boston, MA). To each flash plate 60 μL flash plate buffer was added followed by 40 μL acidified cell sample or cAMP standard, followed with the addition of 100 μl ^{125}I-cAMP trace. The FlashPlates were sealed, incubated overnight @ room temperature, and counted in a Packard TopCount (Packard Instrument Co., Meriden, CT). The cAMP radioimmunoassay results were calculated using DPM conversion and log-logit transformation of % binding (Excel program).

Progesterone and Estradiol Production

The effects of the FSH antagonist on steroid production from rat granulosa cells was used to confirm that the effects on cAMP production also caused changes in progesterone and estradiol production, the biologically relevant steroids in vivo. Granulosa cells prepared as described above were incubated in the absence or presence of test compounds for intervals between 12 and 48 hours to determine the effects of compound on FSH-stimulated progesterone and estradiol production. At the end of incubation the media was aspirated (using a multichannel pipettor) into corresponding microtiter plates, and were stored at –20°C until the concentration of estradiol and progesterone were measured by radioimmunoassay.

Radioimmunoassay of estradiol and progesterone

Concentrations of E and P in media from the same culture wells were measured using [^{125}I]-progesterone and [^{125}I]-estradiol Coat-A-Count radioimmunoassay kits (Diagnostic Products Corp., Los Angeles, CA). According to the manufacturers specification sheets, the anti-progesterone antibody cross-reacts 2% with 20a-dihydroprogesterone, 2.4% with 11-deoxycortisol, 1.7% with 11-deoxycorticosterone, and 1.3% with 5b-pregnan-3,20-dione. The cross-reactivity of pregnenolone, 17a-hydroxyprogesterone, and testosterone was less than 0.4 %. The assay detection limit was 0.03 ng/ml. The anti-estradiol antibody cross-reacts 10% with estrone, 4.4% with equilenin, 1.8% with estrone glucuronide, 0.3% with estriol, and less than 0.1% with other estrogens and androgens. The assay detection limit was 8 pg/ml.

TABLE 6

Cmpd #	Rat Granulosa Cell EC_{50} cAMP (μM)	Cmpd #	Rat Granulosa Cell EC_{50} cAMP (μM)
1	2.42	78	0.57
2	0.34	79	1.60
3	0.21	80	0.23
4	0.29	81	25.23
5	0.27	82	0.12

	6	0.29	83	0.12
	7	0.83	84	7.66
	8	0.31	85	0.35
	9	0.47	86	2.64
5	10	1.39	87	0.19
	11	0.40	88	0.14
	12	0.28	89	1.88
	13	0.48	90	0.90
	14	1.56	91	0.40
10	15	5.55	92	3.08
	16	0.51	93	0.17
	17	0.49	94	8.91
	18	0.36	95	0.32
	19	1.67	96	3.09
15	20	0.64	97	0.55
	21	5.30	98	0.43
	22	0.85	99	0.59
	24	1.07	100	0.32
	25	1.33	101	25.08
20	26	4.30	102	0.17
	27	1.01	103	0.55
	28	1.81	104	32.88
	29	2.06	105	8.00
	30	0.49	106	10.22
25	31	1.97	107	1.90
	32	0.16	108	1.45
	33	0.18	109	3.16
	34	0.17	110	4.89
	35	0.20	111	1.32
30	36	0.49	112	8.63
	37	0.28	113	0.60
	38	1.07	114	8.97
	39	0.52	115	1.02

	40	1.92	117	1.16
	41	0.26	118	2.47
	42	1.45	119	2.95
	43	0.88	120	1.63
5	44	0.72	122	1.53
	45	2.85	123	10.00
	46	6.37	124	1.01
	47	0.55	125	2.80
	48	1.08	126	25.11
10	49	2.06	129	1.29
	50	1.20	131	1.35
	51	3.01	135	1.44
	52	3.50	197	0.06
	53	3.52	198	0.02
15	54	3.22	199	0.06
	55	12.48	200	0.05
	56	5.16	201	0.15
	57	1.92	202	0.15
	58	2.15	203	0.06
20	59	2.07	204	0.19
	60	29.35	205	0.05
	61	7.51	206	0.91
	62	1.27	208	0.04
	63	3.70	214	0.05
25	64	1.46	215	0.01
	65	1.07	257	1.65
	66	4.58	271	2.80
	67	25.68	272	0.60
	68	3.89	275	2.15
30	69	5.86	278	0.47
	70	5.01	358	0.11
	71	3.21	370	0.22
	72	2.19	373	0.11

73	1.45	375	0.08
74	8.23	377	0.09
75	0.20	384	0.08
76	0.94	400	0.03
77	0.44		

EXAMPLE 30

IN VIVO TESTING

Inhibition of FSH-stimulated Ovarian Proliferation

Twenty-one day old immature female Wistar rats (Charles River) are implanted with Alzet pumps (Alza Corp.,) containing human FSH at a concentration calculated to deliver 4 – 8IU hFSH per day. The animals are given vehicle or test compound at a dosage level of 20 mg/kg compound (BID) dissolved in hydroxypropyl methylcellulose (HPMC). On the third or fourth day, blood samples are obtained by orbital puncture for the measurement of serum estrogen and progesterone, and immediately afterwards, ovaries and uterus are collected, weighed and prepared for histological examination. The effect of test compound is determined by measuring the weight of ovaries and uterus collected from animals treated with the test compound as compared with the weight of ovaries and uterus collected from animals treated with vehicle.

Interruption of 4-day estrus cycle

The estrus cycles of mature cycling female Wistar rats (250g) were monitored for 2 consecutive estrus cycles to select animals with regular 4-day estrus cycles. The animals were randomly assigned to treatment groups on the morning of estrus. Starting on the morning of estrus and continuing through 2 estrus cycles, the animals orally dosed with vehicle or test compound at a concentration of 20 mg/kg; BID. At the end of the second estrus cycle, blood samples were collected by orbital puncture on the morning of estrus. The

animals were then sacrificed, and the number of ovulated eggs in the oviduct were counted.

TABLE 7

Cmpd. #	Estradiol Concentration	Progesterone Concentration	# Ovulated Eggs
198	20.1 ± 4.4	3.6 ± 0.9	14.0
215	22.2 ± 4.2	2.6 ± 0.6	16.3
Vehicle	23.8 ± 3.1	8.0 ± 2.7	16.3

Effects on Spermatogenesis in Immature Male Rats

Twenty-one day old immature male Wistar rats (Charles River) were treated with FSH antagonist at a concentration of 20 mg/kg BID for 25 days. On the penultimate day of treatment, blood samples were collected by orbital puncture immediately prior to oral dosing, and 3 hours after dosing into Vacutainers containing EDTA. On the last day of treatment, blood samples were again collected prior to time of compound administration. The concentrations of LH, FSH and testosterone were measured in the plasma. Testosterone was measured using a Coat-A-Count kit (Diagnostic Products Corp.) and luteinizing hormone and follicle stimulating hormone concentrations were measured following previously established. At the end of the treatment period, the animals were sacrificed, testes and prostates were collected and weighed, and the testes were prepared for histological examination. The presence of sperm in testes were evaluated by hematoxylin and eosin staining, and in separate slides with a BERG stain (REF, 1963).

TABLE 8

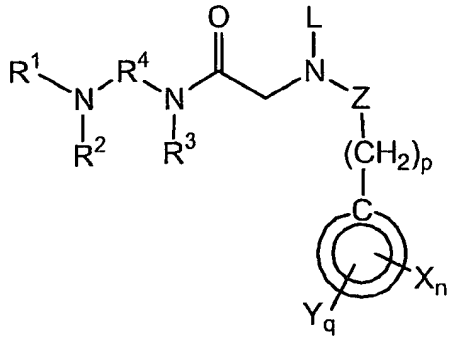
Cmpd. #	Serum Testosterone (t = 3hr, d = 25)	Testes Weight	Prostate Weight	Mating Sperm
198	3.6 ± 0.6	8.8 ± 0.2	1.6 ± 0.2	3 / 4
215	4.9 ± 0.7	8.7 ± 0.5	1.8 ± 0.1	1 / 4

Vehicle	3.2 0.6	7.5 ± 1.6	1.6 ± 0.1	4 / 6

While the foregoing specification teaches the principles of the present invention, with examples provided for the purpose of illustration, it will be understood that the practice of the invention encompasses all of the usual variations, adaptations and/or modifications as come within the scope of the following claims and their equivalents.

We claim:

1. A compound of the formula:



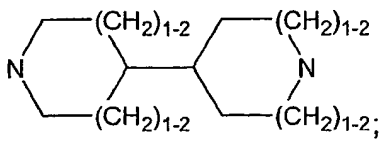
wherein

R^1 and R^2 are independently selected from the group consisting of hydrogen, C_1-C_6alkyl, C_1-C_6alkylcarbonyl, C_1-C_6perhaloalkyl, phenyl, phenyl C_1-C_6alkyl-, phenylcarbonyl-, pyridyl, pyridyl C_1-C_6alkyl-, pyridylcabonyl-, thienyl, thienyl C_1-C_6alkyl- and thienylcarbonyl, wherein the phenyl, pyridyl or thienyl is optionally substituted with one to three substituents independently selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy or NO_2;

R^3 is selected from the group consisting of hydrogen, C_1-C_6alkyl, C_2-C_4alkenyl and C_2-C_4alkynyl, where the C_1-C_6alkyl is optionally substituted with a phenyl, pyridyl, thienyl or furyl, wherein the phenyl, pyridyl, thienyl or furyl is optionally substituted with one to three substituents independently selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy or NO_2;

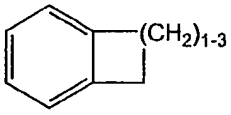
R^4 is selected from the group consisting of $-C_2$-C_6alkyl-, -cyclopentyl-, -cylcohexyl-, -cyclohexyl-CH_2-, -CH_2-cyclohexyl-CH_2-, $-CH_2$-phenyl-CH_2-, -C(O)-CH_2-phenyl-CH_2-, -C(O)-C_1-C_6alkyl- and –cyclohexyl-CH_2-cyclohexyl;

where the R^4 substituent is inserted into the compound of formula (I) from left to right, as defined;

alternately, R^2, R^3, and R^4 can be taken together with the two N atoms of the diamine portion of the molecule to form  ;

alternately, R^3 can be taken together with R^2 as -C_2-C_3alkyl-, provided that R^4 is -C_2-C_6alkyl-;

L is selected from the group consisting of $-C_3$-C_6cycloalkyl (wherein the cycloalkyl is substituted with R^5 and R^6), a bicyclic compound of the form



(wherein the point of the attachment of the bicyclic compound is any carbon atom of the alkyl portion and wherein the aromatic portion of the bicyclic compound is optionally substituted with one to three substituents independently selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy, NO_2, acetamido, $-NH_2$, $-NH(C_1$-C_6alkyl) or $-N(C_1$-C_6alkyl$)_2$), and $-(CH_2)_m$-$CR^8R^5R^6$;

m is 0 to 3;

R^5 is selected from the group consisting of phenyl, naphthyl, (wherein the phenyl and naphthyl may be optionally substituted with one to three substituents independently selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy, NO_2, acetamido, $-NH_2$, $-NH(C_1$-C_6alkyl), $-N(C_1$-C_6alkyl$)_2$, C_1-C_6alkylcarbonylamino or C_1-C_6alkylsulfonylamino), bicyclo[4.2.0]octa-1,3,5-trienyl, 2,3-dihydro-1H-indolyl, N-methylpyrrolidinyl, 3,4-methylenedioxyphenyl, C_3-C_6cyloalkenyl, (wherein the cycloalkenyl group contains one or two double bonds), a six membered heteroaryl (wherein the six membered heteroaryl contains one to three N atoms), and a five membered heteroaryl (wherein the five membered heteroaryl contains one sulfur, oxygen or nitrogen, optionally contains one to three additional nitrogen atoms); wherein the point of attachment for the five or six membered heteroaryl is a carbon atom; and wherein the five or six membered heteroaryl is optionally substituted with one to three substituents independently selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy or NO_2;

R^6 is selected from the group consisting of hydrogen, C_1-C_6alkyl, C_3-C_6cycloalkyl, C_1-C_6alkoxy, hydroxy and phenyl, (wherein the phenyl may be optionally substituted with one to three substituents independently selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl or trifluoromethoxyl); provided that R^6 may be phenyl only when R^5 is phenyl;

R^8 is selected from the group consisting of hydrogen and C_1-C_6alkyl;

Z is selected from the group consisting of $-SO_2$-, -C(=O)-, and

–C(=O)NH-;

p is 0 to 1;

is selected from the group consisting of phenyl, napthyl, quinolinyl, thienyl, and furyl;

X is selected from the group consisting of halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy, NO_2, acetamido, -NH_2, -NH (C_1-C_6alkyl) and -N(C_1-C_6alkyl)$_2$;

n is 0 to 3;

Y is selected from the group consisting of phenyl, -O-phenyl, -NH-phenyl, naphthyl, (wherein the phenyl or naphthyl is optionally substituted with one to three substituents selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy, NO_2, cyano, methylthio, acetamido, formyl, -amino, -aminocarbonyl, -NH C_1-C_6alkyl, -N(C_1-C_6alkyl)$_2$, -COOH, -COO(C_1-C_6alkyl), -COO(C_1-C_6alkylphenyl), C_1-C_6alkylcarbonylamino, C_1-C_6alkylaminocarbonyl, di(C_1-C_6alkyl)aminocarbonyl, aminosulfonyl, C_1-C_6akylaminosulfonyl or di(C_1-C_6alkyl)aminosulfonyl)), biphenyl, 3,4-methylenedioxyphenyl, dianthrenyl, dibenzothienyl, phenoxathiinyl, a six membered heteroaryl (wherein the six membered heteroaryl contains one to three nitrogen atoms), and a five membered heteroaryl (wherein the five membered heteroaryl contains one sulfur, oxygen or nitrogen atom, optionally contains one to three additional nitrogen atoms); wherein the point of attachment for the five or six membered heteroaryl is a carbon atom; and wherein the five or six membered heteroaryl is optionally substituted with one to three substituents selected from halogen, C_1-C_6alkyl, C_1-C_6alkoxy, trifluoromethyl, trifluoromethoxy, formyl, NO_2, cyano, methylthio, acetamido, -amino, -aminocarbonyl, -NH C_1-C_6alkyl, -N(C_1-C_6alkyl)$_2$, -COOH, -COO(C_1-C_6alkyl), or -COO(C_1-C_6alkylphenyl));

q is 0 to 1;

provided that when q is 1, n is 0;

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

2. The compound of Claim 1 wherein

R^1 and R^2 are independently selected from the group consisting of hydrogen, methyl, ethyl, methylcarbonyl, trifluoromethyl, phenyl, benzyl, phenylcarbonyl, pyridyl, pyridylcarbonyl, thienyl, thienylmethyl and thienylcarbonyl (where the phenyl, pyridyl or thienyl is optionally substituted with one to two substituents independently selected from halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl, trifluoromethoxy or nitro); and

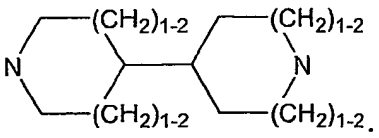
R^3 is selected from the group consisting of hydrogen, methyl, -CH=CH- (optionally substituted with phenyl, pyridyl or thienyl; wherein the phenyl, pyridyl or thienyl is further optionally substituted with one to two substituents independently selected from the group consisting of halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl, trifluoromethoxy and nitro), -C≡C-, (optionally substituted with phenyl, pyridyl or thienyl; wherein the phenyl, pyridyl or thienyl is further optionally substituted with one to two substituents independently selected from the group consisting of halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl, trifluoromethoxy and nitro).

3. The compound of Claim 1 wherein R^1, R^2, and R^3 are the same and are hydrogen.

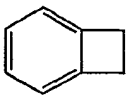
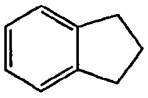
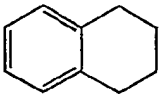
4. The compound of Claim 1 wherein one of R^1 or R^2 is other than hydrogen.

5. The compound of Claim 1 wherein R^2 and R^3 are taken together as C_2-C_3alkyl and R^4 is C_2-C_6alkyl.

6. The compound of Claim 1 wherein R^2, R^3, and R^4 are taken together with the two N atoms of the diamine portion of the molecule to form



7. The compound of Claim 1 wherein R^4 is selected from the group consisting of $-C_2$-C_6alkyl, -cyclohexyl, -CH_2-cyclohexyl-CH_2, -cyclohexyl-CH_2-cyclohexyl- and $-CH_2$-phenyl-CH_2-.

8. The compound of Claim 1 wherein L is selected from the group consisting of –cyclopropyl-, cyclohexyl-, (wherein the cyclopropyl or cyclohexyl is substituted with R^5 and R^6),  ,  ,  , and $(CH_2)_m$-$CR^8R^5R^6$.

9. The compound of Claim 1 wherein R^5 is selected from the group consisting of phenyl (wherein the phenyl is optionally substituted with one to two substituents independently selected from halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl, trifluoromethoxy, methylcarbonylamino, methylsulfonylamino, nitro, acetomido, amino, C_1-C_3alkylamino or di(C_1-C_3alkyl)amino), N-methylpyrrolidinyl, 3,4-methylenedioxyphenyl, bicyclo[4.2.0]octa-1,3,5-trienyl, 2,3-dihydro-1H-indolyl, C_3-C_6cycloalkenyl (wherein the cycloalkenyl contains one or two double bonds), thienyl, furyl, pyrrolyl, oxazolyl, imidazolyl, pyrazolyl, triazolyl, pyridyl, pyrimidyl, pyrazinyl and triazinyl.

10. The compound of Claim 1 wherein R^6 is selected from the group consisting of hydrogen, C_1-C_3alkyl, cyclopropyl, cyclobutyl, cyclohexyl, C_1-C_3alkoxy, hydroxy and phenyl (wherein the phenyl is optionally substituted with one to two substituents independently selected from halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl or trifluoromethoxy); provided that R^6 is phenyl only when R^5 is phenyl.

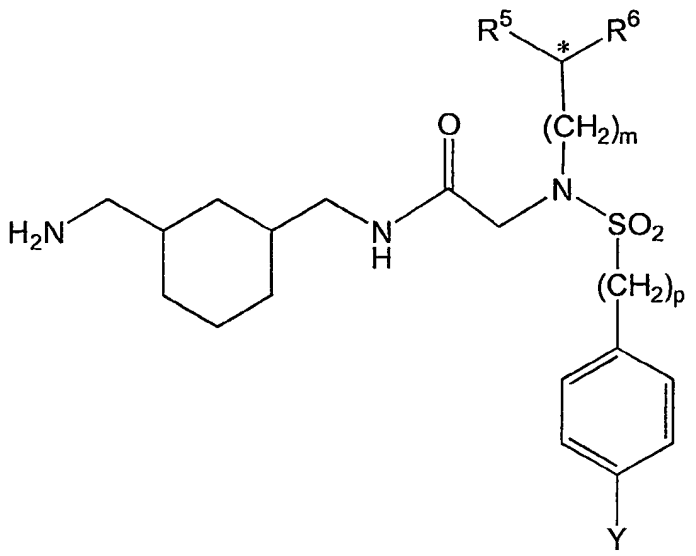
11. The compound of Claim 1 wherein R^8 is selected from the group consisting of hydrogen and C_1-C_3alkyl.

12. The compound of Claim 1 wherein  is selected from the group consisting of phenyl, naphthyl, quinolinyl and thienyl.

13. The compound of Claim 1 wherein X is selected from the group consisting of halogen, C_1-C_6alkyl, C_1-C_4alkoxy, trifluoromethyl, trifluoromethoxy, nitro, acetamido, amino, C_1-C_3alkylamino and di(C_1-C_3alkyl)amino.

14. The compound of Claim 1 wherein Y is selected from the group consisting of phenyl, naphthyl (wherein the phenyl or naphthyl is optionally substituted with one to three substituents independently selected from halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl, trifluoromethoxy, formyl, nitro, cyano, methylthio, acetamido, amino, aminocarbonyl, C_1-C_3alkylamino, di(C_1-C_3alkyl)amino, carboxy, -COO(C_1-C_3alkyl), -COO(C_1-C_3alkylphenyl), C_1-C_4alkylaminosulfonyl or C_1-C_4alkylcarbonylamino), 3,4-methylenedioxyphenyl, dianthryl, dibenzothienyl, phenoxathiinyl, a five membered heteroaryl (wherein the five membered heteroaryl contains one nitrogen, oxygen or sulfur atom and optionally contains an additional nitrogen or oxygen atom) and a six membered heteroaryl (wherein the six membered heteroaryl contains one nitrogen atom and optionally contains an additional nitrogen or oxygen atom); wherein the five or six membered heteroaryl is optionally substituted with one to two substituents independently selected from halogen, C_1-C_3alkyl, C_1-C_3alkoxy, trifluoromethyl, trifluoromethoxy, formyl, nitro, cyano, methylthio, acetamido, amino, aminocarbonyl, C_1-C_3alkylamino or di(C_1-C_3alkyl)amino; and wherein the point of attachment for the five or six membered heteroaryl is a carbon atom.

15. The compound of Claim 1 of the formula

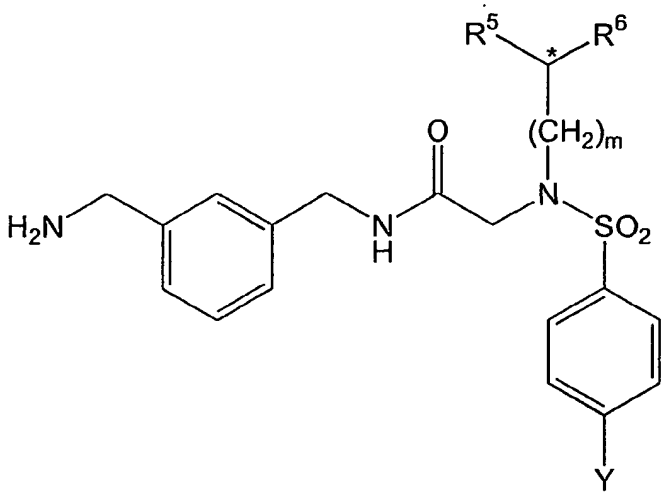


wherein m, R^5, R^6, p, Y and the stereospecificity are selected in concert from the group consisting of:

m	R^5	R^6	Stereo	p	Y
1	2-methoxyphenyl	H	-	0	2-methylphenyl
1	2-methoxyphenyl	H	-	0	2-chlorophenyl
1	2-methoxyphenyl	H	-	0	2-methoxyphenyl
1	2-methoxyphenyl	H	-	0	2,4-dichlorophenyl
0	2-methoxyphenyl	H	-	0	2-methylphenyl
0	2-methoxyphenyl	H	-	0	2-chlorophenyl
0	2-methoxyphenyl	H	-	0	2-methoxyphenyl
0	2-methoxyphenyl	H	-	0	2,4-dichlorophenyl
1	phenyl	CH_3	R	0	2-methylphenyl
1	phenyl	CH_3	R	0	2-chlorophenyl
1	phenyl	CH_3	R	0	3-fluorophenyl
1	phenyl	CH_3	S	0	2-methylphenyl
1	phenyl	CH_3	S	0	2-chlorophenyl
1	phenyl	CH_3	S	0	3-fluorophenyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

16. The compound of Claim 1 of the formula

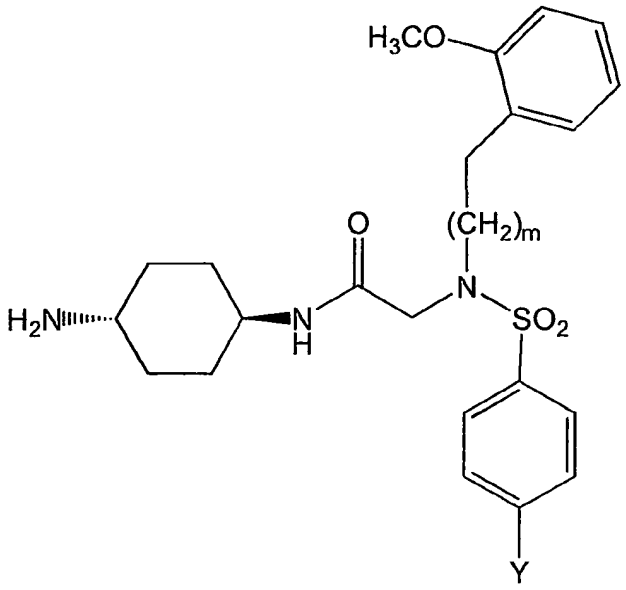


wherein m, R^5, R^6, p, Y and the stereospecificity are selected in concert from the group consisting of:

m	R^5	R^6	Stereo	p	Y
1	2-methoxyphenyl	H	-	0	2-methylphenyl
1	2-methoxyphenyl	H	-	0	2-chlorophenyl
1	2-methoxyphenyl	H	-	0	2-methoxyphenyl
1	2-methoxyphenyl	H	-	0	2,4-dichlorophenyl
0	2-methoxyphenyl	H	-	0	2-methyl
0	2-methoxyphenyl	H	-	0	2-chlorophenyl
0	2-methoxyphenyl	H	-	0	2-methoxyphenyl
0	2-methoxyphenyl	H	-	0	2,4-dichlorophenyl
1	phenyl	CH_3	R	0	2-methylphenyl
1	phenyl	CH_3	R	0	2-chlorophenyl
1	phenyl	CH_3	R	0	3-fluorophenyl
1	phenyl	CH_3	S	0	2-methylphenyl
1	phenyl	CH_3	S	0	2-chlorophenyl
1	phenyl	CH_3	S	0	3-fluorophenyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

17. The compound of Claim 1 of the formula



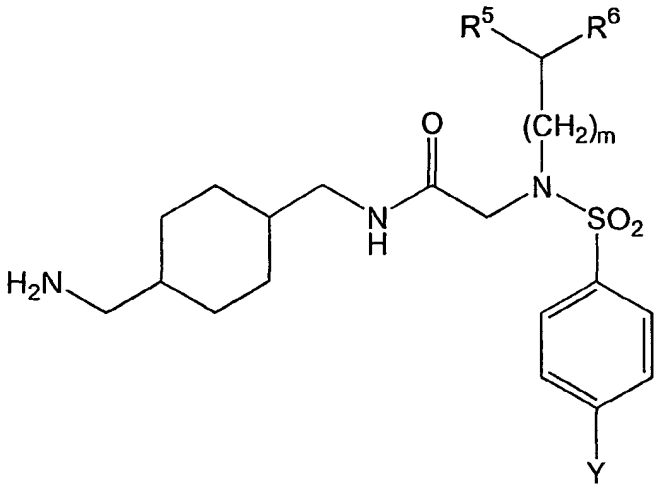
wherein m and Y are selected in concert from the group consisting of:

m	Y
0	2-methylphenyl
0	3-thienyl
0	2-methoxyphenyl
0	4-fluorophenyl
0	2,3-dimethoxyphenyl
0	4-methoxyphenyl
0	4-methylphenyl
0	1-napthyl
0	2-chlorophenyl
0	3-pyridyl
0	2-thienyl
0	3-aminocarbonylphenyl
0	phenyl
0	4-chlorophenyl
0	4-[3,5-dimethylisoxazolyl]
0	2-furyl
0	4-cyanophenyl
0	4-pyridyl
0	3-methoxyphenyl

0	4-aminophenyl
1	2-methylphenyl
1	3-thienyl
1	2-methoxyphenyl
1	4-fluorophenyl
1	2,3-dimethyoxyphenyl
1	4-methoxyphenyl
1	4-methylphenyl
1	1-napthyl
1	2-chlorophenyl
1	3-pyridyl
1	2-thienyl
1	3-aminocarbonylphenyl
1	phenyl
1	4-chlorophenyl
1	4-[3,4-dimethylisoxazolyl]
1	2-furyl
1	4-cyano phenyl
1	4-pyridyl
1	3-methoxyphenyl
1	4-aminophenyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

18. The compound of Claim 1 of the formula



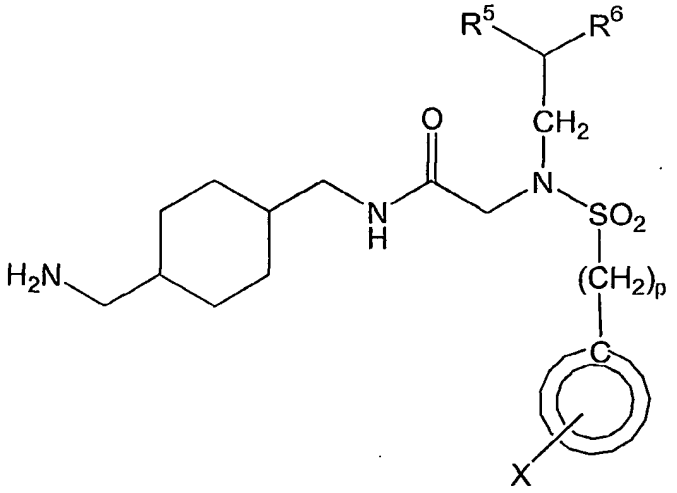
wherein m, R^5, R^6 and Y are selected in concert from the group consisting of:

m	R^5	R^6	Y
0	2-methoxyphenyl	H	4-chlorophenyl
0	2-methoxyphenyl	H	3-trifluoromethylphenyl
0	2-methoxyphenyl	H	2-chlorophenyl
0	2-methoxyphenyl	H	2-methylphenyl
0	2-methoxyphenyl	H	2-methoxyphenyl
0	2-methoxyphenyl	H	2,4-dichlorophenyl
0	2-methoxyphenyl	H	3,5-di(trifluoromethyl)phenyl
0	2-methoxyphenyl	H	3-chloro-4-fluorophenyl
0	2-methoxyphenyl	H	4-methoxyphenyl
0	3-methoxyphenyl	H	3-trifluoromethylphenyl
0	3-methoxyphenyl	H	2-methoxyphenyl
0	3-methoxyphenyl	H	2,4-dichlorophenyl
0	3-methoxyphenyl	H	3-fluorophenyl
0	3-methoxyphenyl	H	3-methoxyphenyl
0	3-methoxyphenyl	H	4-methylphenyl
0	3-methoxyphenyl	H	4-fluorophenyl
0	3-methoxyphenyl	H	3-chloro-4-fluorophenyl
0	3-methoxyphenyl	H	4-methoxyphenyl
1	2-methoxyphenyl	H	3-trifluoromethyl phenyl
1	2-methoxyphenyl	H	3-nitrophenyl

1	2-methoxyphenyl	H	2-chlorophenyl
1	2-methoxyphenyl	H	2-methylphenyl
1	2-methoxyphenyl	H	2-methoxyphenyl
1	2-methoxyphenyl	H	2,4-dichlorophenyl
1	2-methoxyphenyl	H	phenyl
1	2-methoxyphenyl	H	3-chlorophenyl
1	2-methoxyphenyl	H	4-fluorophenyl
1	2-methoxyphenyl	H	2-trifluoromethyl phenyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

19. The compound of Claim 1 of the formula



wherein R^5, R^6, p,  , and X are selected in concert from the group consisting of:

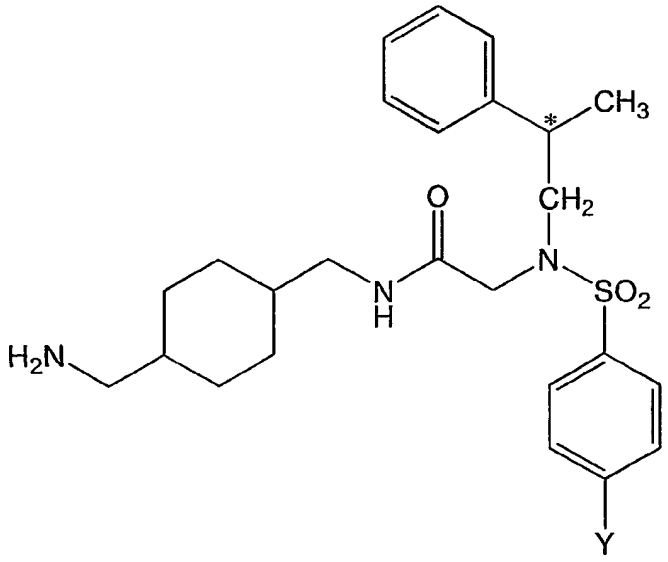
R^5	R^6	p	C	X
2-methoxyphenyl	H	0	phenyl	-
2-methoxyphenyl	H	0	2-thienyl	5-chloro
2-methoxyphenyl	H	0	1-phenyl	3-trifluoromethyl
2-methoxyphenyl	H	0	1-phenyl	2-trifluoromethyl
2-methoxyphenyl	H	0	1-phenyl	3-chloro

2-methoxyphenyl	H	0	1-phenyl	3,4-dichloro
2-methoxyphenyl	H	0	2-napthyl	-
2-methoxyphenyl	H	0	1-phenyl	2-chloro
2-methoxyphenyl	H	0	1-phenyl	4-chloro
2-methoxyphenyl	H	0	3-thienyl	2,5-dichloro
2-methoxyphenyl	H	0	1-phenyl	2,4-dichloro
2-methoxyphenyl	H	0	1-phenyl	2,6-dichloro
2-methoxyphenyl	H	0	1-phenyl	3,5-dichloro
2-methoxyphenyl	H	0	1-phenyl	2,5-dichloro
2-methoxyphenyl	H	0	1-phenyl	2,3-dichloro
2-methoxyphenyl	H	1	phenyl	-
2-methoxyphenyl	H	0	1-phenyl	4-methyl
2-methoxyphenyl	H	0	1-phenyl	4-methoxy
2-methoxyphenyl	H	0	1-napthyl	-
2-methoxyphenyl	H	0	1-phenyl	4-fluoro
2-methoxyphenyl	H	0	1-phenyl	3,4-dimethoxy
2-methoxyphenyl	H	0	1-phenyl	2,5-dimethoxy
2-methoxyphenyl	H	0	1-phenyl	2-nitro
2-methoxyphenyl	H	0	1-phenyl	4-nitro
2-methoxyphenyl	H	0	1-phenyl	3-nitro
2-methoxyphenyl	H	0	1-phenyl	4-iodo
2-methoxyphenyl	H	0	1-phenyl	4-tert-butyl
2-methoxyphenyl	H	0	1-phenyl	2-nitro-4-methoxy
2-methoxyphenyl	H	0	1-phenyl	3-methyl-4-methoxy
2-methoxyphenyl	H	0	1-phenyl	2-nitro-4-trifluoromethyl
2-methoxyphenyl	H	0	1-phenyl	3-fluoro

2-methoxyphenyl	H	0	1-phenyl	2-fluoro
2-methoxyphenyl	H	0	1-phenyl	4-trifluoromethyl
2-methoxyphenyl	H	0	1-phenyl	4-trifluoromethoxy
2-methoxyphenyl	H	0	1-phenyl	2,3-dichloro
3,4-methylenedioxyphenyl	H	0	8-quinolinyl	-

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

20. The compound of Claim 1 of the formula

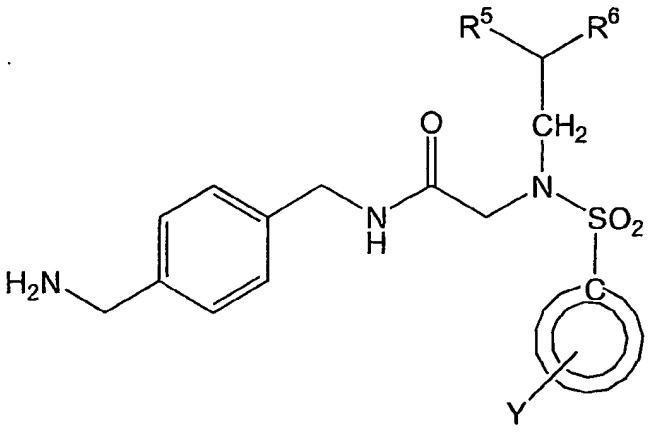


wherein the stereospecificity and Y are selected in concert from the group consisting of:

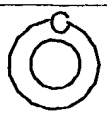
Stereo	Y
R	2-methylphenyl
R	2-chlorophenyl
R	3-fluorophenyl
S	2-methylphenyl
S	2-chlorophenyl
S	3-fluorophenyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

21. The compound of Claim 1 of the formula



wherein R^5, R^6,  , Y and stereospecificity are selected in concert from the group consisting of:

R^5	R^6	Stereo		Y
2-methoxyphenyl	H	-	1,4-phenyl	3-nitrophenyl
2-methoxyphenyl	H	-	1,4-phenyl	2-chlorophenyl
2-methoxyphenyl	H	-	1,4-phenyl	2-methylphenyl
2-methoxyphenyl	H	-	1,4-phenyl	2-methoxy phenyl
2-methoxyphenyl	H	-	1,4-phenyl	3-fluorophenyl
2-methoxyphenyl	H	-	1,4-phenyl	phenyl
2-methoxyphenyl	H	-	1,4-phenyl	3-methoxy phenyl
2-methoxyphenyl	H	-	1,4-phenyl	4-fluorophenyl
2-methoxyphenyl	H	-	1,4-phenyl	2-trifluoromethylphenyl
2-methoxyphenyl	H	-	1,4-phenyl	3-chloro-4-fluorophenyl
phenyl	CH_3	R	1,4-phenyl	phenyl
phenyl	CH_3	S	1,4-phenyl	phenyl
phenyl	CH_3	S	1,4-phenyl	2-chlorophenyl
phenyl	CH_3	S	1,4-phenyl	3-chlorophenyl
phenyl	CH_3	S	1,4-phenyl	2-methoxyphenyl
phenyl	CH_3	S	1,4-phenyl	3-methoxyphenyl
phenyl	CH_3	S	1,4-phenyl	4-methoxyphenyl
phenyl	CH_3	S	1,4-phenyl	3-fluorophenyl

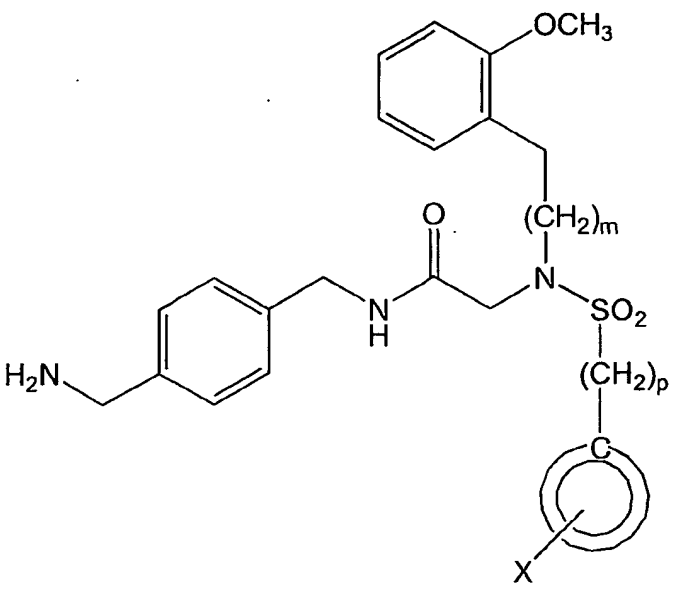
phenyl	CH_3	S	1,4-phenyl	4-fluorophenyl
phenyl	CH_3	S	1,4-phenyl	2-methylphenyl
phenyl	CH_3	S	1,4-phenyl	4-methylphenyl
2-methoxyphenyl	H	-	1,2-phenyl	2-thienyl
2-methoxyphenyl	H	-	1,2-phenyl	2-methylphenyl
2-methoxyphenyl	H	-	1,2-phenyl	3-thienyl
2-methoxyphenyl	H	-	1,2-phenyl	2-methoxyphenyl
2-methoxyphenyl	H	-	1,2-phenyl	4-fluorophenyl
2-methoxyphenyl	H	-	1,2-phenyl	4-methoxyphenyl
2-methoxyphenyl	H	-	1,2-phenyl	4-methylphenyl
2-methoxyphenyl	H	-	1,2-phenyl	1-napthyl
2-methoxyphenyl	H	-	1,2-phenyl	4-chlorophenyl
2-methoxyphenyl	H	-	1,2-phenyl	3-methoxy phenyl
2-methoxyphenyl	H	-	1,2-phenyl	3-aminophenyl
2-methoxyphenyl	H	-	1,2-phenyl	3-fluorophenyl
2-methoxyphenyl	H	-	1,2-phenyl	2-fluorophenyl
2-methoxyphenyl	H	-	1,2-phenyl	1-(3,4-methylene dioxyphenyl)
2-methoxyphenyl	H	-	1,2-phenyl	phenyl
2-methoxyphenyl	H	-	1,2-phenyl	4-(3,5-dimethyl isoxazole)
2-methoxyphenyl	H	-	1,2-phenyl	4-cyanophenyl
2-methoxyphenyl	H	-	1,2-phenyl	4-pyridyl
2-methoxyphenyl	H	-	1,2-phenyl	2,3,4-trimethoxyphenyl
2-methoxyphenyl	H	-	1,2-phenyl	3-cyanophenyl
2-methoxyphenyl	H	-	1,2-phenyl	2,5-dimethoxyphenyl
2-methoxyphenyl	H	-	1,2-phenyl	2,4-dichlorophenyl
2-methoxyphenyl	H	-	1,2-phenyl	3-trifluoromethylphenyl
2-methoxyphenyl	H	-	1,2-phenyl	4-trifluoromethylphenyl
2-methoxyphenyl	H	-	1,2-phenyl	2-trifluoromethylphenyl
2-methoxyphenyl	H	-	1,2-phenyl	3-methylphenyl
2-methoxyphenyl	H	-	1,3-phenyl	2-methylphenyl
2-methoxyphenyl	H	-	1,3-phenyl	3-thienyl

2-methoxyphenyl	H	-	1,3-phenyl	2-methoxyphenyl
2-methoxyphenyl	H	-	1,3-phenyl	4-fluorophenyl
2-methoxyphenyl	H	-	1,3-phenyl	4-methoxyphenyl
2-methoxyphenyl	H	-	1,3-phenyl	4-methoxyphenyl
2-methoxyphenyl	H	-	1,3-phenyl	1-napthyl
2-methoxyphenyl	H	-	1,3-phenyl	3-pyridyl
2-methoxyphenyl	H	-	1,3-phenyl	4-chlorophenyl
2-methoxyphenyl	H	-	1,3-phenyl	3-methoxyphenyl
2-methoxyphenyl	H	-	1,3-phenyl	3-aminophenyl
2-methoxyphenyl	H	-	1,3-phenyl	3-fluorophenyl
2-methoxyphenyl	H	-	1,3-phenyl	2-fluorophenyl
2-methoxyphenyl	H	-	1,3-phenyl	1-(3,4-methylene dioxyphenyl)
2-methoxyphenyl	H	-	1,3-phenyl	3-chlorophenyl
2-methoxyphenyl	H	-	1,3-phenyl	phenyl
2-methoxyphenyl	H	-	1,3-phenyl	4-(3,5-dimethyl isoxazole)
2-methoxyphenyl	H	-	1,3-phenyl	4-cyanophenyl
2-methoxyphenyl	H	-	1,3-phenyl	4-pyridyl
2-methoxyphenyl	H	-	1,3-phenyl	2,3,4-trimethoxyphenyl
2-methoxyphenyl	H	-	1,3-phenyl	4-cyanophenyl
2-methoxyphenyl	H	-	1,3-phenyl	2,5-dimethoxyphenyl
2-methoxyphenyl	H	-	1,3-phenyl	3-trifluoromethylphenyl
2-methoxyphenyl	H	-	1,3-phenyl	4-trifluoromethylphenyl
2-methoxyphenyl	H	-	1,3-phenyl	2-trifluoromethylphenyl
2-methoxyphenyl	H	-	1,3-phenyl	3-methylphenyl
2-methoxyphenyl	H	-	2,5-thienyl	2-thienyl
2-methoxyphenyl	H	-	2,5-thienyl	2-methylphenyl
2-methoxyphenyl	H	-	2,5-thienyl	3-thienyl
2-methoxyphenyl	H	-	2,5-thienyl	2-methoxyphenyl
2-methoxyphenyl	H	-	2,5-thienyl	4-fluorophenyl
2-methoxyphenyl	H	-	2,5-thienyl	4-methoxyphenyl
2-methoxyphenyl	H	-	2,5-thienyl	4-methylphenyl

2-methoxyphenyl	H	-	2,5-thienyl	2-chlorophenyl
2-methoxyphenyl	H	-	2,5-thienyl	3-pyridyl
2-methoxyphenyl	H	-	2,5-thienyl	4-chlorophenyl
2-methoxyphenyl	H	-	2,5-thienyl	3-methoxyphenyl
2-methoxyphenyl	H	-	2,5-thienyl	3-aminophenyl
2-methoxyphenyl	H	-	2,5-thienyl	3-fluorophenyl
2-methoxyphenyl	H	-	2,5-thienyl	2-fluorophenyl
2-methoxyphenyl	H	-	2,5-thienyl	3-chlorophenyl
2-methoxyphenyl	H	-	2,5-thienyl	phenyl
2-methoxyphenyl	H	-	2,5-thienyl	4-(3,5-dimethyl isoxazole)
2-methoxyphenyl	H	-	2,5-thienyl	4-cyanophenyl
2-methoxyphenyl	H	-	2,5-thienyl	4-pyridyl
2-methoxyphenyl	H	-	2,5-thienyl	2,3,4,-trimethoxyphenyl
2-methoxyphenyl	H	-	2,5-thienyl	3-cyanophenyl
2-methoxyphenyl	H	-	2,5-thienyl	2-furyl
2-methoxyphenyl	H	-	2,5-thienyl	2,5-dimethoxyphenyl
2-methoxyphenyl	H	-	2,5-thienyl	2,4-dichlorophenyl
2-methoxyphenyl	H	-	2,5-thienyl	3-trifluoromethylphenyl
2-methoxyphenyl	H	-	2,5-thienyl	4-trifluoromethylphenyl
2-methoxyphenyl	H	-	2,5-thienyl	2-trifluoromethylphenyl
2-methoxyphenyl	H	-	2,5-thienyl	3-methylphenyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

22. The compound of Claim 1 of the formula



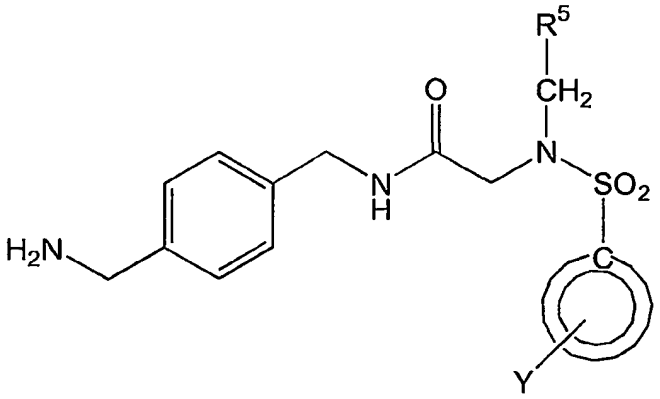
wherein p, m,  and X are selected in concert from the group consisting of:

p	m		X
0	1	2-thienyl	5-chloro
0	1	phenyl	3-trifluoromethyl
0	1	phenyl	2-trifluoromethyl
0	1	phenyl	3-chloro
0	1	phenyl	3,4-dichloro
0	1	2-napthyl	-
0	1	phenyl	2-chloro
0	1	phenyl	2,5-dimethoxy
0	1	phenyl	2,4-dichloro
0	1	phenyl	2,6-dichloro
0	1	phenyl	2,5-dichloro
0	1	phenyl	3,5-dichloro
0	1	2-thienyl	4,5-dichloro
1	1	phenyl	-
0	1	phenyl	4-methoxy

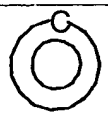
0	1	1-napthyl	-
0	1	phenyl	4-fluoro
0	1	phenyl	3-fluoro
0	1	phenyl	2-fluoro
0	1	phenyl	3,4-dimethoxy
0	1	phenyl	2-nitro
0	1	phenyl	3-nitro
0	1	phenyl	4-nitro
0	1	phenyl	4-iodo
0	1	phenyl	4-t-butyl
0	1	phenyl	2-nitro-4-methoxy
0	1	phenyl	2-methoxy-5-methyl
0	1	2-thienyl	4-nitro-5-chloro
0	1	phenyl	2-nitro-4-trifluoro methyl
0	1	phenyl	4-trifluoromethyl
0	1	phenyl	4-trifluoromethoxy
0	1	2-thienyl	-
0	1	phenyl	4-methyl
0	1	phenyl	4-chloro
0	1	phenyl	-
0	0	1-phenyl	2,3-dichloro

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

23. The compound of Claim 1 of the formula

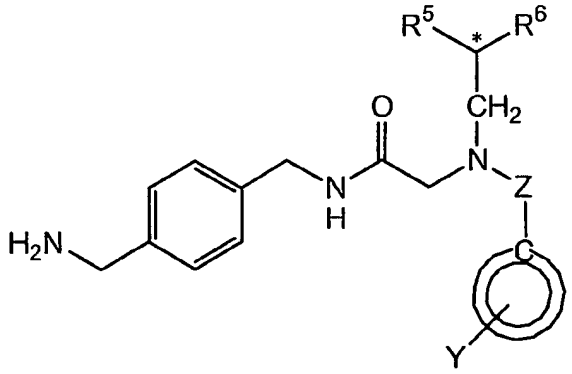


wherein R^5,  and Y are selected in concert from the group consisting of:

R^5		Y
2-methoxyphenyl	2,-thienyl	5-(2-methylthio-pyrimidyl)
3,4-methylenedioxyphenyl	8-quinolinyl	-

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

24. The compound of Claim 1 of the formula



wherein R^5, R^6, Z,  , Y and the stereospecificity are selected in concert from the group consisting of:

R^5	R^6	Stereo	Z		Y
2-methoxy phenyl	H	-	SO_2	2,5-thienyl	2-pyridyl
2-methoxy phenyl	H	-	SO_2	2,5-thienyl	5-(2-methylthio-pyrimidyl)
phenyl	CH_3	R	SO_2	1,4-phenyl	2-chlorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-chlorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-methoxyphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-methoxyphenyl

phenyl	CH_3	R	SO_2	1,4-phenyl	4-methoxyphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-fluorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	4-fluorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-methylphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	4-methylphenyl
2-methoxy phenyl	H	-	SO_2	1,2-phenyl	3-chlorophenyl
2-methoxy phenyl	H	-	SO_2	1,3-phenyl	2-chlorophenyl
2-methoxy phenyl	H	-	SO_2	2,5-thienyl	1-naphthyl
2-methoxy phenyl	H	-	SO_2	2,5-thienyl	1-(3,4-methylene dioxyphenyl)
phenyl	CH_3	R	SO_2	1,4-phenyl	2-fluorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2,6-dichlorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2,4-dichlorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-trifluoromethyl phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2,4,6-trimethyl phenyl
phenyl	CH_3	S	SO_2	1,4-phenyl	2-fluorophenyl
phenyl	CH_3	S	SO_2	1,4-phenyl	2,6-difluorophenyl
phenyl	CH_3	S	SO_2	1,4-phenyl	2,4-dichlorophenyl
phenyl	CH_3	S	SO_2	1,4-phenyl	2-trifluoromethyl phenyl
phenyl	CH_3	S	SO_2	1,4-phenyl	2,4,6-trimethylphenyl
phenyl	CH_3	Mix	SO_2	1,4-phenyl	2-methylphenyl
phenyl	CH_3	Mix	SO_2	1,4-phenyl	2-chlorophenyl
phenyl	CH_3	Mix	SO_2	1,4-phenyl	3-fluorophenyl
4-chlorophenyl	CH_3	Mix	SO_2	1,4-phenyl	2-methylphenyl
4-chlorophenyl	CH_3	Mix	SO_2	1,4-phenyl	2-chlorophenyl
4-chlorophenyl	CH_3	Mix	SO_2	1,4-phenyl	3-fluorophenyl
4-chlorophenyl	cyclo-	-	SO_2	1,4-phenyl	2-methylphenyl

4-chlorophenyl	propyl cyclo-propyl	-	SO_2	1,4-phenyl	2-chlorophenyl
4-chlorophenyl	cyclo-propyl	-	SO_2	1,4-phenyl	3-fluorophenyl
phenyl	H	-	SO_2	1,4-phenyl	2-methylphenyl
phenyl	H	-	SO_2	1,4-phenyl	2-chlorophenyl
phenyl	H	-	SO_2	1,4-phenyl	3-fluorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-nitrophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	4-fluorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-methylphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-trifluoromethyl phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	4-trifluoromethyl phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-chlorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-methoxy phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-trifluoromethyl phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-methoxy phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	4-trifluoro methoxyphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-fluorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-naphthyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-chloro-4-fluorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-bromophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	4-chlorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3,5-dichloro phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2,4-dichloro phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3,5-ditrifluoro methylphenyl

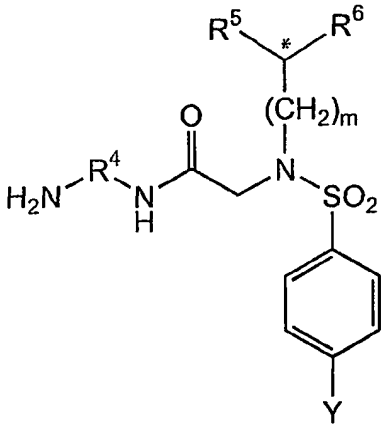
phenyl	CH_3	R	SO_2	1,4-phenyl	2-benzofuryl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-(t-butylamino sulfonyl)phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	4-cyanophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-cyanophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-carboxyphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2[(di-i-propyl) aminocarbonyl] phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	4-(3,5-dimethyl) isoxazolyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-methoxy-5-formylphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	4-pyridyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2,3,4-tri methoxyphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	phenoxathiinyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-(5-formyl)furyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-(4-methyl) thienyl
phenyl	CH_3	R	SO_2	1,4-phenyl	dibenzothienyl
phenyl	CH_3	R	SO_2	1,4-phenyl	dianthrenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	dibenzothienyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-benzothienyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3,4-dimethoxy phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-fluorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	1-naphthyl
phenyl	CH_3	R	SO_2	1,4-phenyl	4-methoxy phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-fluoro-4-chlorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-nitrophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-biphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-(t-butylcarbonyl

					amino)-3-methoxy phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-(t-butyl carbonyl amino)-5-methoxy phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-(5-formyl)furyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2,5-dimethoxy phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-(di(i-propyl) aminocarbonyl)-3-methoxyphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	4-methylthio phenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2,4,6-tri methylphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-methylphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	4-methylphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-pyridyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-aminophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-methylcarbonyl aminophenyl
phenyl	CH_3	R	C(O)	1,4-phenyl	2-chlorophenyl
phenyl	CH_3	R	C(O)	1,4-phenyl	2-methylphenyl
phenyl	CH_3	R	C(O)	1,4-phenyl	3-fluorophenyl
phenyl	CH_3	R	C(O)	1,4-phenyl	2-bromophenyl
phenyl	CH_3	R	C(O)	1,4-phenyl	2,5-dichlorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-methyl-3-chlorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-chloro-5-methylphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-methyl-5-chlorophenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	3-chloro-4-methylphenyl

phenyl	CH_3	R	SO_2	1,4-phenyl	2-chloro-6-methylphenyl
phenyl	CH_3	R	SO_2	1,4-phenyl	2-chloro-4-methylphenyl
3-trifluoro methylphenyl	H	-	SO_2	1,4-phenyl	phenyl
phenyl	CH_3	R	C(O)NH	1,4-phenyl	phenyl
phenyl	CH_3	S	C(O)NH	1,4-phenyl	phenyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

25. The compound of Claim 1 of the formula



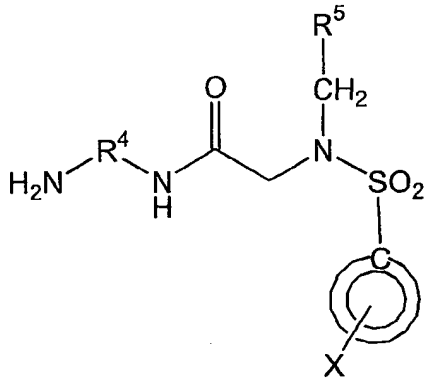
wherein R^4, m, R^5, R^6, Y and the stereospecificity are selected in concert from the group consisting of:

R^4	m	R^5	R^6	Stereo	Y
1,5-n-pentyl	1	phenyl	CH_3	R	2-methylphenyl
1,5-n-pentyl	1	phenyl	CH_3	R	2-chlorophenyl
1,5-n-pentyl	1	phenyl	CH_3	R	3-fluorophenyl
1,5-n-pentyl	1	phenyl	CH_3	S	2-methylphenyl
1,5-n-pentyl	1	phenyl	CH_3	S	2-chlorophenyl
1,5-n-pentyl	1	phenyl	CH_3	S	3-fluorophenyl
1,5-n-pentyl	1	2-methoxyphenyl	H	-	2-methylphenyl
1,6-n-hexyl	1	2-methoxyphenyl	H	-	2-chlorophenyl
1,6-n-hexyl	1	2-methoxyphenyl	H	-	2-methoxyphenyl
1,6-n-hexyl	1	2-methoxyphenyl	H	-	2,4-dichlorophenyl

1,6-n-hexyl	0	2-methoxyphenyl	H	-	2-methylphenyl
1,6-n-hexyl	0	2-methoxyphenyl	H	-	2-chlorophenyl
1,6-n-hexyl	0	2-methoxyphenyl	H	-	2-methoxyphenyl
1,6-n-hexyl	0	2-methoxyphenyl	H	-	2,4-dichlorophenyl
1,6-n-hexyl	1	phenyl	CH_3	R	2-methylphenyl
1,6-n-hexyl	1	phenyl	CH_3	R	2-chlorophenyl
1,6-n-hexyl	1	phenyl	CH_3	R	3-fluorophenyl
1,6-n-hexyl	1	phenyl	CH_3	S	2-methylphenyl
1,6-n-hexyl	1	phenyl	CH_3	S	2-chlorophenyl
1,6-n-hexyl	1	phenyl	CH_3	S	3-fluorophenyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

26. The compound of Claim 1 of the formula

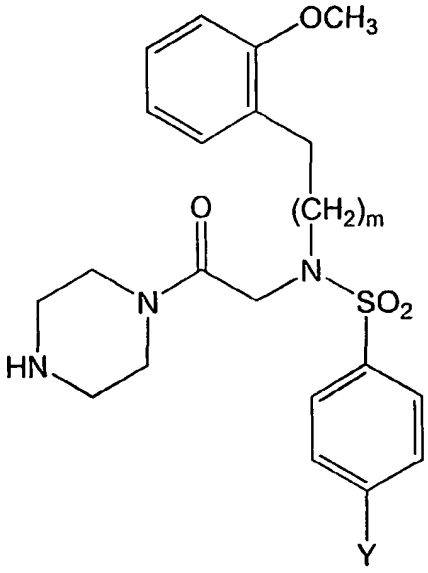


wherein R^4, R^5,  and X are selected in concert from the group consisting of:

R^4	R^5		X
1,4-n-butyl	2-methoxyphenyl	1-phenyl	2,3-dichloro
1,6-n-hexyl	2-methoxyphenyl	1-phenyl	2,3-dichloro
1,4-n-butyl	3,4-methylenedioxyphenyl	8-quinolinyl	-
1,6-n-hexyl	3,4-methylenedioxyphenyl	8-quinolinyl	-

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

27. The compound of Claim 1 of the formula



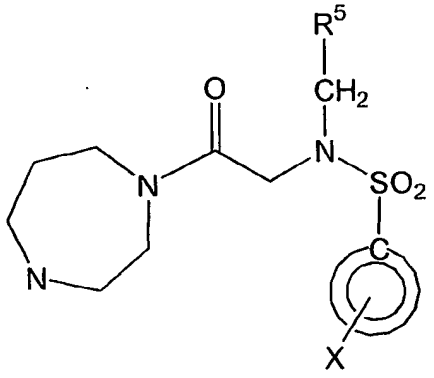
wherein m and Y are selected in concert from the group consisting of:

m	Y
1	2-methylphenyl
1	3-thienyl
1	2-methoxyphenyl
1	4-fluorophenyl
1	2,4-dimethoxyphenyl
1	4-methoxyphenyl
1	4-methylphenyl
1	1-napthyl
1	2-chlorophenyl
1	3-pyridyl
1	2-thienyl
1	3-acetamidophenyl
1	phenyl
1	4-chlorophenyl
1	4-[3,5-dimethylisoxazolyl]
1	3-chlorophenyl
1	4-cyanophenyl
1	4-pyridyl

1	3-methoxyphenyl
1	3-aminophenyl
1	3-fluorophenyl
1	2-fluorophenyl
1	3,4-methylenedioxyphenyl
0	2-methylphenyl
0	3-thienyl
0	2-methoxyphenyl
0	4-fluorophenyl
0	2,4-dimethoxyphenyl
0	4-methoxyphenyl
0	4-methylphenyl
0	1-napthyl
0	2-chlorophenyl
0	3-pyridyl
0	2-thienyl
0	3-acetamidophenyl
0	phenyl
0	4-chlorophenyl
0	4-[3,5-dimethylisoxazolyl]
0	3-chlorophenyl
0	4-cyanophenyl
0	4-pyridyl
0	3-methoxyphenyl
0	3-aminophenyl
0	3-fluorophenyl
0	2-fluorophenyl
0	3,4-methylenedioxyphenyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

28. The compound of Claim 1 of the formula

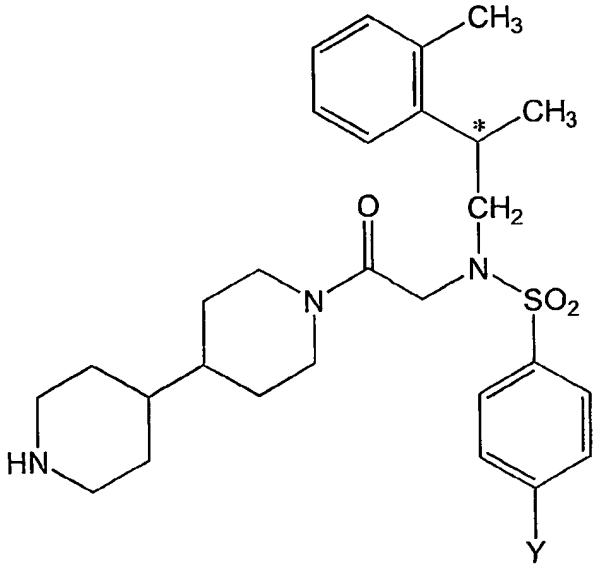


wherein R^5,  and X are selected in concert from the group consisting of:

R^5		X
2-methoxyphenyl	1-phenyl	2,3-dichloro
3,4-methylenedioxyphenyl	8-quinolinyl	-

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

29. The compound of Claim 1 of the formula



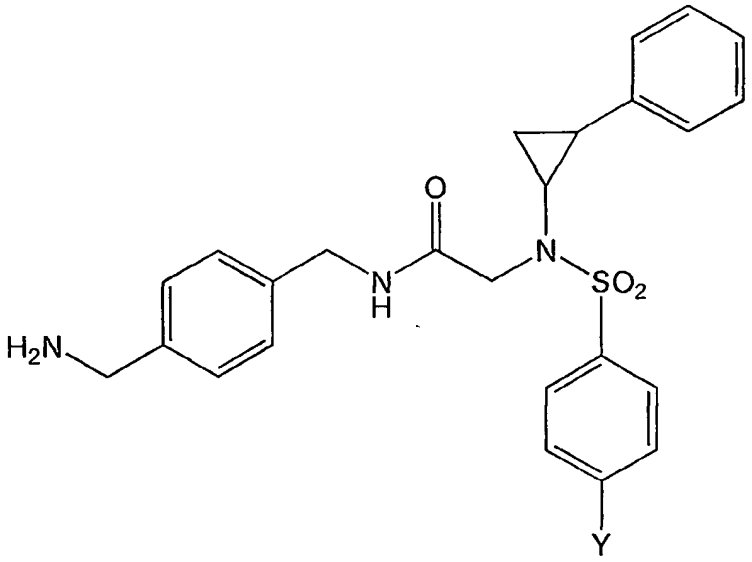
wherein Y and the stereospecificity are selected in concert from the group consisting of:

Stereo	Y

R	2-methylphenyl
R	2-chlorophenyl
R	3-fluorophenyl
S	2-methylphenyl
S	2-chlorophenyl
S	3-fluorophenyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

30. The compound of Claim 1 of the formula

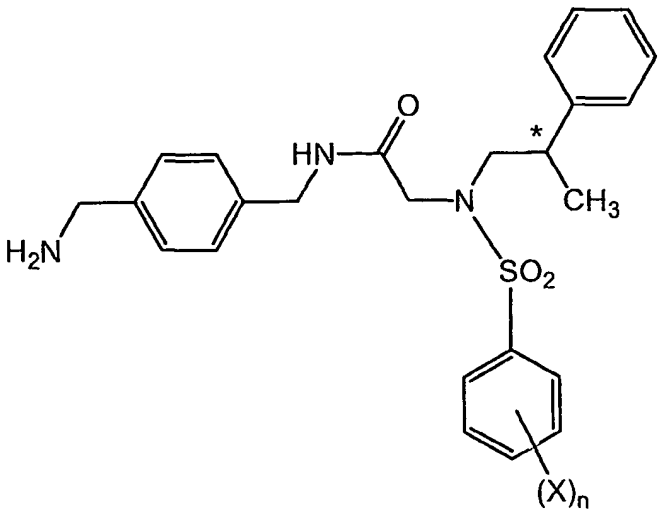


wherein Y is from the group consisting of:

Y
2-methylphenyl
2-chlorophenyl
3-fluorophenyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

31. The compound of Claim 1 of the formula



wherein X and n and the stereospecificity are selected in concert from the group consisting of:

Stereo	n	X
R	1	4-n-butyl
R	0	-
R	1	4-bromo
S	1	4-bromo
R	1	4-methoxy
R	1	4-trifluoromethyl
R	1	4-isopropyl
R	1	4-n-propyl
R	1	4-t-butyl
R	1	4-n-pentyl
R	1	3-methoxy
S	1	4-methoxy
S	1	4-trifluoromethyl
S	1	4-isopropyl
S	1	4-n-propyl
S	1	4-t-butyl
S	1	4-n-pentyl
S	1	3-methoxy

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

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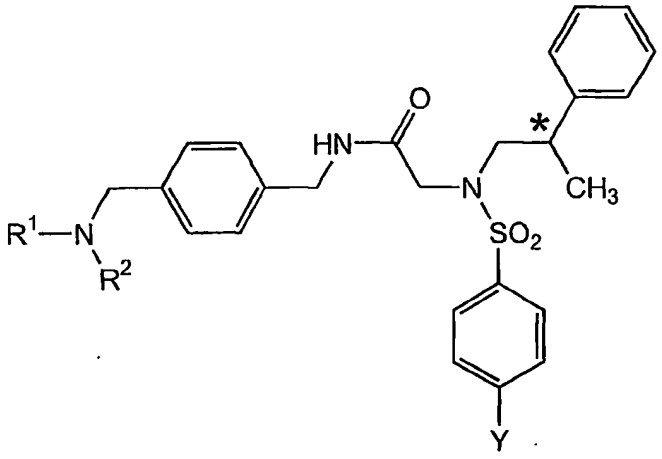
32. The compound of Claim 1 of the formula

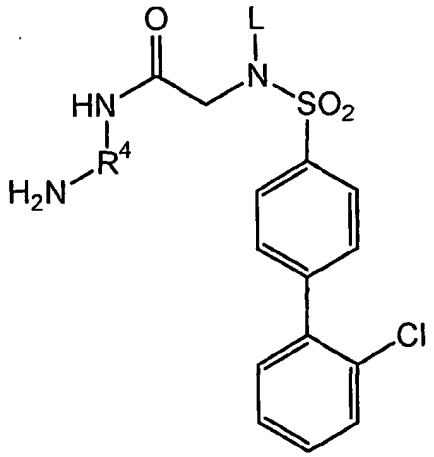


wherein R^1, R^2, Y and the stereospecificity are selected in concert from the group consisting of:

R^1	R^2	Stereo	Y
methyl	methyl	R	2-chlorophenyl
ethyl	ethyl	R	2-chlorophenyl
H	methylcarbonyl	R	2-chlorophenyl
methyl	methyl	S	2-methylphenyl
ethyl	ethyl	S	2-methylphenyl
H	methylcarbonyl	S	2-methylphenyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

33. The compound of Claim 1 of the formula



wherein R^4 and L are selected in concert from the group consisting of

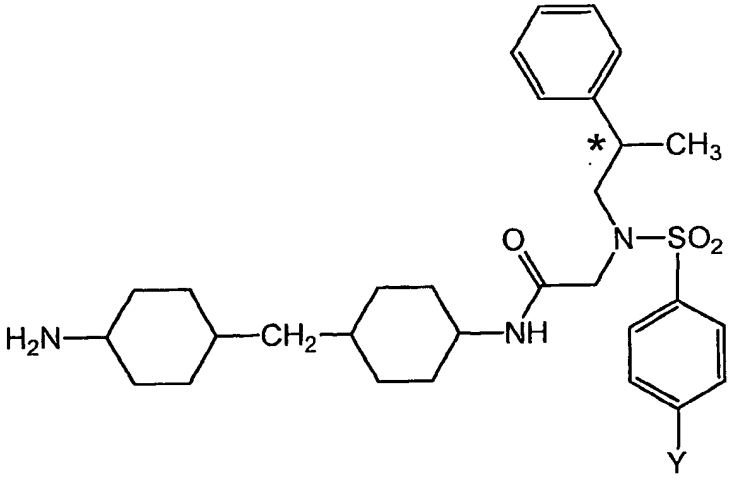
R^4	L
-CH_2-(1,4-phenyl)-CH_2-	4-methyoxyphenylethyl
-CH_2-(1,4-phenyl)-CH_2-	3,6-dimethoxyphenylethyl
-CH_2-(1,4-phenyl)-CH_2-	2,3-dimethoxyphenylethyl
-CH_2-(1,4-phenyl)-CH_2-	1-cyclohexenylethyl
-CH_2-(1,4-phenyl)-CH_2-	3-bromo-4,5-dimethylphenylethyl
-CH_2-(1,4-phenyl)-CH_2-	2-chlorphenylethyl
-CH_2-(1,4-phenyl)-CH_2-	3-chlorophenylethyl
-CH_2-(1,4-phenyl)-CH_2-	2,4-dichlorophenylethyl
-CH_2-(1,4-phenyl)-CH_2-	2,6-dichlorophenylethyl
-CH_2-(1,4-phenyl)-CH_2-	2-trifluoromethylphenylethyl
-CH_2-(1,4-phenyl)-CH_2-	3,4-dimethylphenylethyl
-CH_2-(1,4-phenyl)-CH_2-	3,5-dimethylphenylethyl
-CH_2-(1,4-phenyl)-CH_2-	3-methoxyphenylethyl
-CH_2-(1,4-phenyl)-CH_2-	3-(2-chlorophenyl)-4,5-dimethoxyphenylethyl
n-hexyl	3,4-dimethoxyphenylethyl
n-hexyl	4-methoxyphenylethyl
n-hexyl	2,3-dimethoxyphenylethyl
n-hexyl	3-bromo-4,5-dimethoxyphenylethyl
n-hexyl	2-chlorophenylethyl
n-hexyl	3-chlorophenylethyl
n-hexyl	2,4-dichlorophenylethyl
n-hexyl	2,6-dichlorophenylethyl
n-hexyl	3,5-dimethoxyphenylethyl
n-hexyl	3-methoxyphenylethyl
n-hexyl	2,5-dimethoxyphenylethyl
n-hexyl	1-cyclohexenylethyl
n-hexyl	3-(2-chlorophenyl)-3,4-dimethoxyphenylethyl
n-hexyl	2-fluorophenylethyl
n-hexyl	2-trifluoromethylphenylethyl

-CH_2-(1,4-phenyl)-CH_2-	2-nitrophenylethyl
-CH_2-(1,4-phenyl)-CH_2-	2-aminophenylethyl
-CH_2-(1,4-phenyl)-CH_2-	2-dimethylaminophenylethyl
-CH_2-(1,4-phenyl)-CH_2-	2-(methylcarbonylamino) phenylethyl
-CH_2-(1,4-phenyl)-CH_2-	2-(methylsulfonylamino) phenylethyl
-CH_2-(1,4-phenyl)-CH_2-	CH_2-$C(CH_3)_2$-phenyl
-CH_2-(1,4-phenyl)-CH_2-	CH_2-$C(OCH_3)$-phenyl
-CH_2-(1,4-phenyl)-CH_2-	CH_2-$CH(CH_3)$-(2-methoxyphenyl)
-CH_2-(1,4-phenyl)-CH_2-	bicyclo[4.2.0]octa-1,3,5-triene
-CH_2-(1,4-phenyl)-CH_2-	CH_2-CH(cyclohexyl)-phenyl
-CH_2-(1,4-phenyl)-CH_2-	CH_2-CH(cyclobutyl)-phenyl
-CH_2-(1,4-phenyl)-CH_2-	CH_2-CH(ethyl)-phenyl
-CH_2-(1,4-phenyl)-CH_2-	2,3-dihydro-1H-indene
-CH_2-(1,4-phenyl)-CH_2-	$CH(phenyl)_2$
-CH_2-(1,4-phenyl)-CH_2-	2-methylphenylethyl
-CH_2-(1,4-phenyl)-CH_2-	3-fluorophenylethyl
-CH_2-(1,4-phenyl)-CH_2-	3,4-methylenedioxy phenyl
-CH_2-(1,4-phenyl)-CH_2-	2-pyridylethyl
-CH_2-(1,4-phenyl)-CH_2-	2-thienylethyl
-CH_2-(1,4-phenyl)-CH_2-	2-(N-methyl)-pyrrolidinylethyl
-CH_2-(1,4-phenyl)-CH_2-	phenylpropyl
-CH_2-(1,4-phenyl)-CH_2-	2-ethoxyphenylethyl
-CH_2-(1,4-phenyl)-CH_2-	3,4-dichlorophenylethyl
n-hexyl	CH_2-$CH(OCH_3)$-phenyl
n-hexyl	CH_2-$CH(CH_3)$-(2-methoxyphenyl)
n-hexyl	bicyclo[4.2.0]octa-1,3,5-triene
n-hexyl	CH_2-CH(cyclohexyl)-phenyl
n-hexyl	CH_2-CH(cyclobutyl)-phenyl
n-hexyl	CH_2-CH(ethyl)-phenyl
n-hexyl	2,3-dihydro-1H-indene
n-hexyl	CH_2-$CH(phenyl)_2$

n-hexyl	2-methylphenylethyl
n-hexyl	3-fluorophenylethyl
n-hexyl	3,4-methylenedioxyphenyl
n-hexyl	2-pyridylethyl
n-hexyl	2-thienylethyl
n-hexyl	2-(N-methylpyrrolidinyl)ethyl
n-hexyl	phenylpropyl
n-hexyl	2-ethoxyphenylethyl
n-hexyl	3,4-dichlorophenylethyl
n-hexyl	3-trifluoromethylphenylethyl

and stereoisomers and pharmaceutically acceptable salts or esters thereof.

34. The compound of Claim 1 of the formula

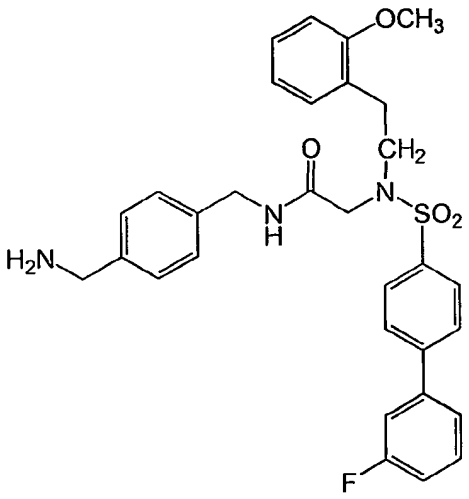


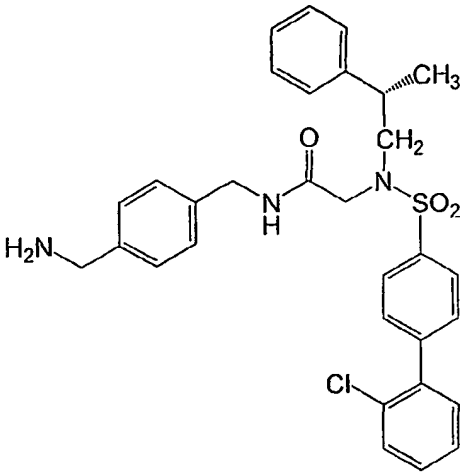
wherein Y and the stereospecificity are selected in concert from the group consisting of:

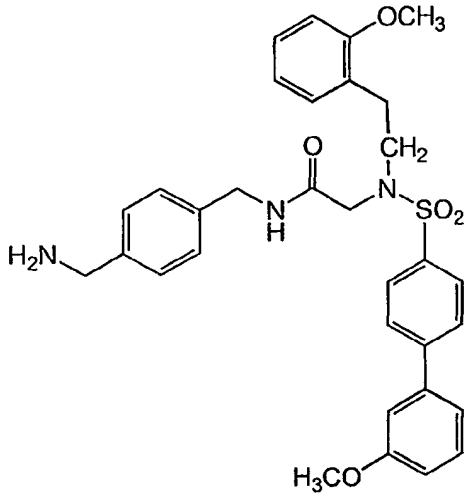
Stereo	Y
R	2-chlorophenyl
R	2-methylphenyl
R	3-fluorophenyl
S	2-chlorophenyl

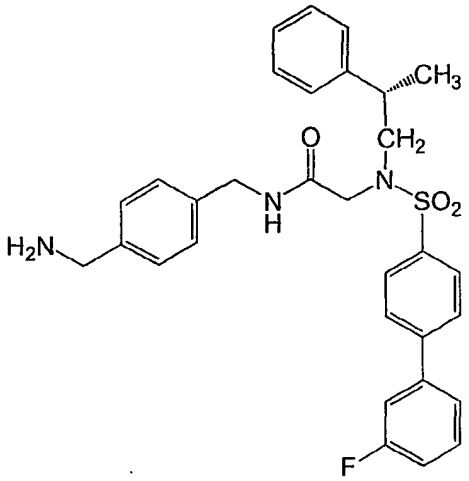
and stereoisomers and pharmaceutically acceptable salts or esters thereof.

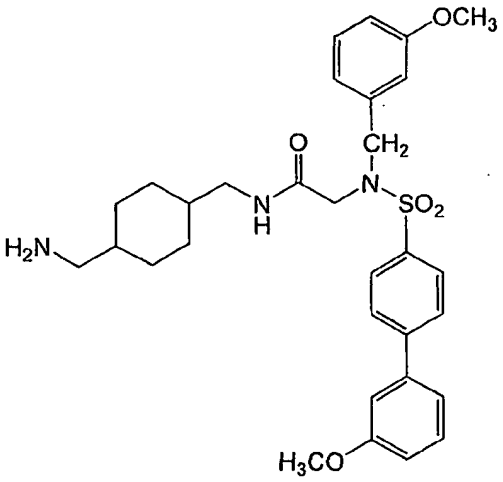
35. The compound of Claim 1, selected from the group consisting of

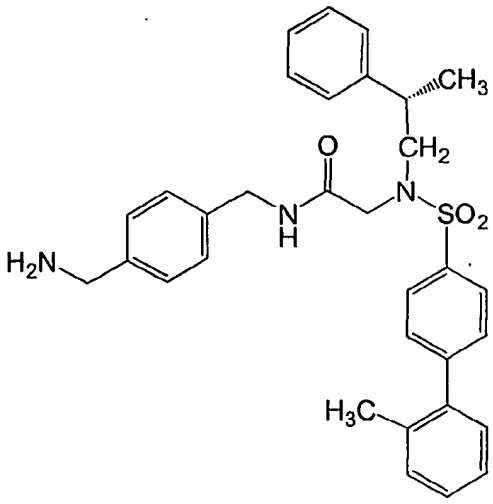


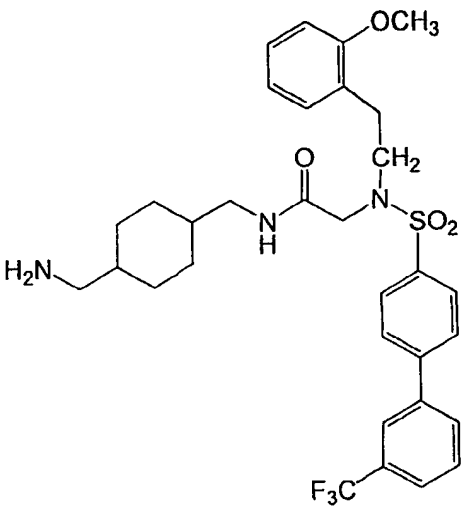


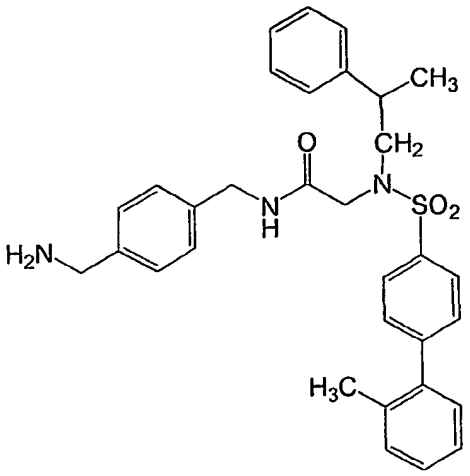


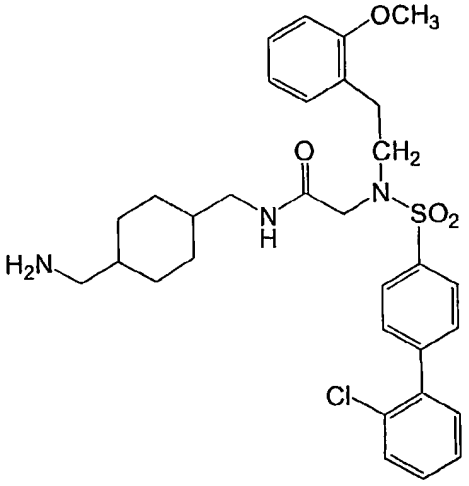


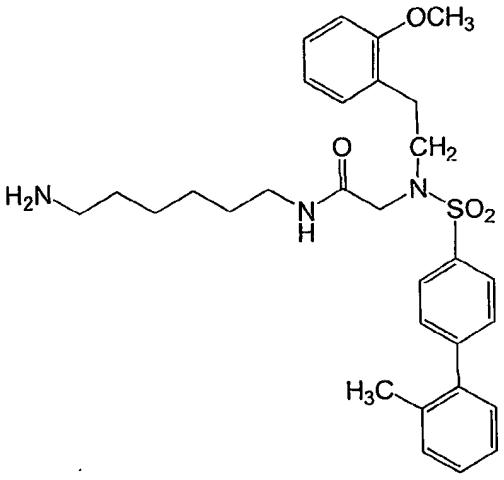


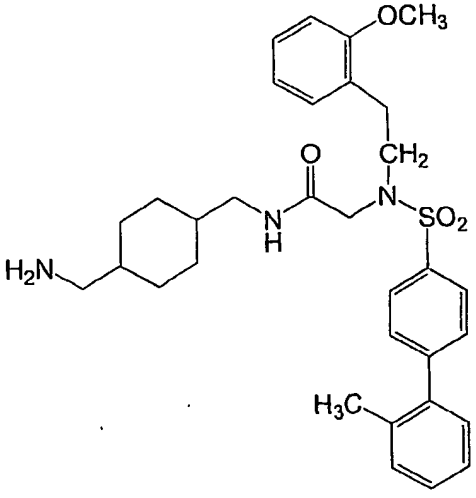


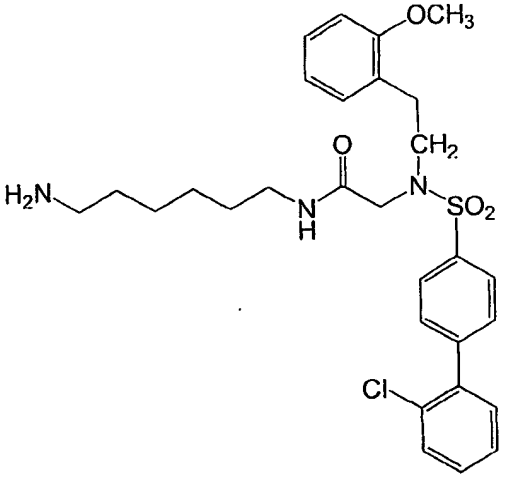


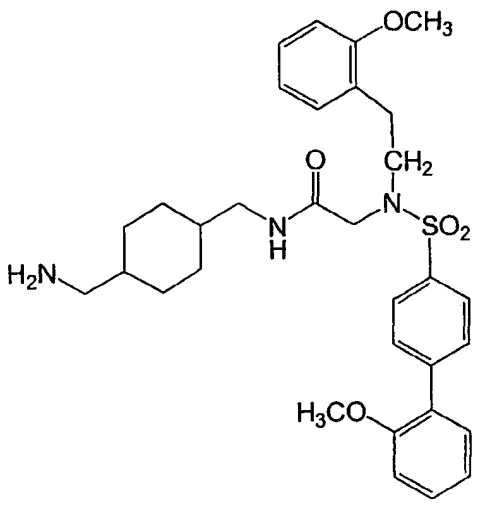


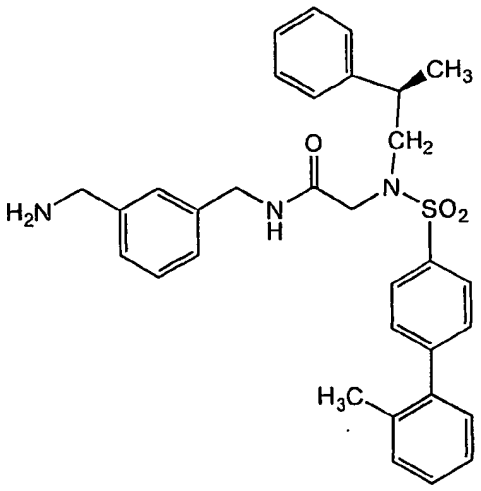


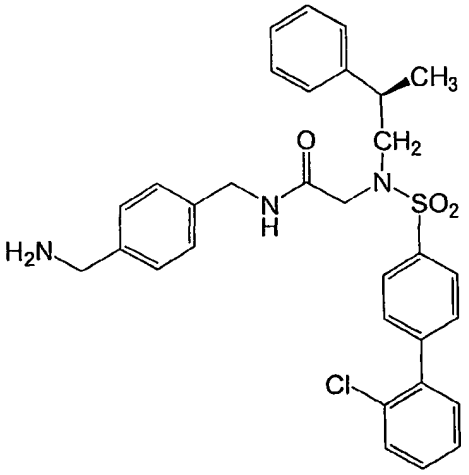


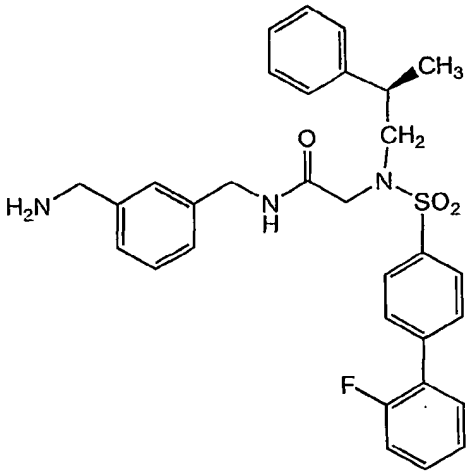


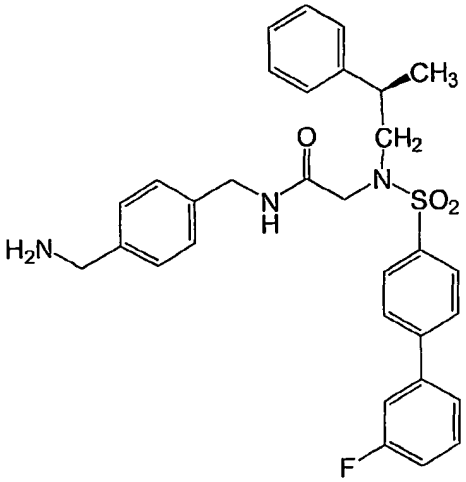


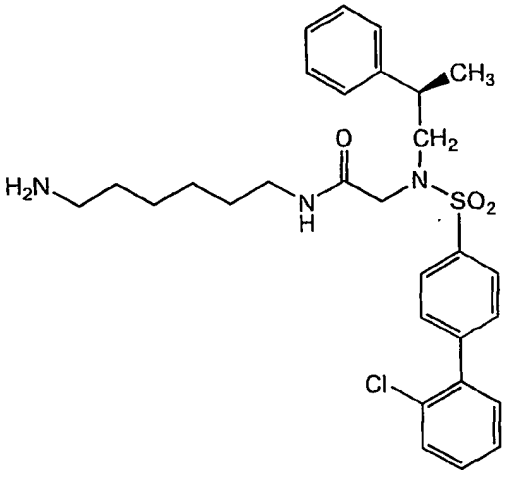












and stereoisomers and pharmaceutically acceptable salts or esters thereof.

36. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of Claim 1.

37. A process for making a pharmaceutical composition comprising mixing a compound of Claim 1 and a pharmaceutically acceptable carrier.

38. A method of treating a condition or disorder mediated by the FSH receptor, in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the compound of Claim 1.

39. A method of treating a condition or disorder selected from the group consisting of uterine fibroids, endometriosis, polycystic ovarian disease, dysfunctional uterine bleeding, breast cancer and ovarian cancer; depletion of oocytes; spermatocyte depletion; or for female and male contraception, in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the compound of Claim 1.

40. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of Claim 1, for the preparation of a medicament for the treatment of a condition or disorder selected from the group consisting of uterine fibroids, endometriosis, polycystic ovarian disease, dysfunctional uterine bleeding, breast cancer and ovarian cancer; depletion of oocytes; spermatocyte depletion; or for female and male contraception.

INTERNATIONAL SEARCH REPORT

Int nal Application No
PCT/US 00/34730

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07C311/19 C07C311/29 C07D333/18 C07D213/34 C07D261/08
C07D307/38 C07C311/42 C07D333/34 A61K31/18 A61K31/33

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07C C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data, BEILSTEIN Data, EPO-Internal, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 93 05014 A (PHARNOWEDROPHARM GMBH) 18 March 1993 (1993-03-18) cited in the application page 1, lines 11-25; pages 23, 25, 27, 29	1,36,37
A	M. CALDARELLI ET AL: BIOORG. MED. CHEM. LETT., vol. 9, no. 14, 1999, pages 2049-2052, XP004171635 table 1, compounds 26-34	1,36,37
A	Y. ZHANG ET AL: BIOORG. MED. CHEM. LETT., vol. 9, no. 19, 1999, pages 2823-2826, XP004179171 tables 1-3	1,36,37

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 March 2001	16/03/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Van Amsterdam, L

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Inte nal Application No
PCT/US 00/34730

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 12038 A (THE BABRAHAM INSTITUTE) 3 April 1997 (1997-04-03) cited in the application	

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INTERNATIONAL SEARCH REPORT

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Int ional Application No
PCT/US 00/34730

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